UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _to_

Commission File Number 001-36352

AKEBIA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**20-8756903**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
245 First Street, Cambridge, MA	**02142**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 871-2098

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.00001 per share	AKBA	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated Filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

Indicate by check mark whether registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the registrant's Common Stock on The Nasdaq Global Market on June 30, 2021, was $632,302,577.

The number of shares of registrant's Common Stock outstanding as of February 23, 2022 was 181,231,071.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2022 Annual Meeting of Stockholders within 120 days after the end of the registrant's fiscal year ended December 31, 2021. Portions of the proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that are being made pursuant to the provisions of the U.S. Private Securities Litigation Reform Act of 1995 with the intention of obtaining the benefits of the "safe harbor" provisions of that Act. All statements contained in this Annual Report on Form 10-K other than statements of historical fact are forward-looking statements. These forward-looking statements may be accompanied by words such as "anticipate," "believe," "build," "can," "contemplate," "continue," "could," "should," "designed," "estimate," "project," "expect," "forecast," "future," "goal," "intend," "likely," "may," "plan," "possible," "potential," "predict," "strategy," "seek," "target," "will," "would," and other words and terms of similar meaning, but the absence of these words does not necessarily mean that a statement is not forward-looking. These forward-looking statements include, but are not limited to, statements about:

- the potential therapeutic benefits, safety profile, and effectiveness of vadadustat;
- the potential for vadadustat to become the new oral standard of care for treatment of adult patients with anemia due to chronic kidney disease;
- that delivering value broadly to the kidney community, as well as others who may benefit from our medicines, will result in delivering value for shareholders;
- the timing of or likelihood of regulatory filings and approvals, including with respect to labeling or other restrictions, the potential approval of vadadustat and our outlook related thereto, and potential indications for vadadustat;
- the timing, investment and associated activities involved in continued commercialization of Auryxia® (ferric citrate), its growth opportunities and our ability to execute thereon;
- the potential indications, demand and market opportunity, potential and acceptance of Auryxia and vadadustat, if approved, including the size of eligible patient populations;
- the potential therapeutic applications of the hypoxia inducible factor pathway;
- our pipeline and portfolio, including its potential, and our related research and development activities;
- our competitive position, including estimates, developments and projections relating to our competitors and their products and product candidates, and our industry;
- our expectations, projections and estimates regarding our capital requirements, need for additional capital, financing our future cash needs, costs, expenses, revenues, capital resources, cash flows, financial performance, profitability, tax obligations, liquidity, growth, contractual obligations, the period of time our cash resources and collaboration funding will fund our current operating plan, our internal control over financial reporting and disclosure controls and procedures, and remediation of the material weakness we have identified in our internal control over financial reporting relating to our inventory process or any future deficiencies or material weaknesses in our internal controls and procedures;
- the direct or indirect impacts of the coronavirus 2 (SARS-CoV-2) pandemic on our business, operations and the markets and communities in which we and our partners, collaborators, vendors, and customers operate;
- our manufacturing, supply and quality matters and any recalls, write-downs, impairments or other related consequences or potential consequences;
- estimates, beliefs and judgments related to the valuation of intangible assets, goodwill, contingent consideration, debt and other assets and liabilities, including our impairment analysis and our methodology and assumptions regarding fair value measurements;
- the timing of the availability and disclosure of clinical trial data and results;
- our and our collaborators' strategy, plans and expectations with respect to the development, manufacturing, supply, commercialization, launch, marketing and sale of Auryxia and vadadustat, if approved, and the associated timing thereof;
- the designs of our studies, and the type of information and data expected from our studies and the expected benefits thereof;
- our ability to maintain any marketing authorizations we currently hold or will obtain, including our marketing authorizations for Auryxia and our ability to complete post-marketing requirements with respect thereto;
- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms and processes on a timely basis, or at all, with third-party payors for Auryxia and vadadustat, if approved;
- the targeted timing of enrollment of our clinical trials;
- the timing of initiation of our clinical trials and plans to conduct preclinical studies and clinical trials in the future;

- the timing and amounts of payments from or to our collaborators and licensees, and the anticipated arrangements and benefits under our collaboration and license agreements, including with respect to milestones and royalties;
- our intellectual property position, including obtaining and maintaining patents, and the timing, outcome and impact of administrative, regulatory, legal and other proceedings relating to our patents and other proprietary and intellectual property rights, patent infringement suits that we have filed or may file, or other actions that we may take against companies, and the timing and resolution thereof;
- expected ongoing reliance on third parties, including with respect to the development, manufacturing, supply and commercialization of Auryxia and vadadustat, if approved;
- accounting standards and estimates, their impact, and their expected timing of completion;
- estimated periods of performance of key contracts;
- our facilities, lease commitments, and future availability of facilities;
- cybersecurity;
- insurance coverage;
- remediation of our material weakness;
- management of personnel, including our management team, and our employees, including employee compensation, employee relations, and our ability to attract, train and retain high quality employees;
- the implementation of our business model, current operating plan, and strategic plans for our business, product candidates and technology, and business development opportunities including potential collaborations, alliances, mergers, acquisitions or licensing of assets; and
- the timing, outcome and impact of current and any future legal proceedings.

Any or all of these forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. These forward-looking statements involve risks and uncertainties, including those that are discussed below under the heading "Risk Factor Summary," and the risk factors detailed further in Part I, Item 1A. "Risk Factors" included in this Annual Report on Form 10-K and elsewhere in this Annual Report on Form 10-K and in our Securities and Exchange Commission reports filed after this report, that could cause our actual results, financial condition, performance or achievements to be materially different from those indicated in these forward-looking statements. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Forward-looking statements speak only as of the date of this Annual Report on Form 10-K. Except as required by law, we assume no obligation to publicly update or revise these forward-looking statements for any reason. Unless otherwise stated, our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

This Annual Report on Form 10-K also contains estimates and other information concerning our industry and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

In this Annual Report on Form 10-K, unless otherwise stated or the context otherwise requires, references to “Akebia,” “we,” “us,” “our,” “the Company,” and similar references refer to Akebia Therapeutics, Inc. and, where appropriate, its subsidiaries, including Keryx.

AURYXIA®, AKEBIA Therapeutics®, Vafseo™ and their associated logos are trademarks of Akebia and/or its affiliates. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners. All website addresses given in this Annual Report on Form 10-K are for information only and are not intended to be an active link or to incorporate any website information into this document.

RISK FACTORS SUMMARY

Investing in our common stock involves numerous risks, including the risks summarized below and described in further detail in "Part I, Item 1A. Risk Factors" of this Annual Report on Form 10-K, any one of which could materially adversely affect our business, financial condition, results of operations, and prospects. These risks include, but are not limited to, the risks noted below.

- Our business is substantially dependent on the commercial success of Auryxia® (ferric citrate) and the regulatory approval and commercial success of vadadustat. If we do not obtain regulatory approval for vadadustat in the United States on a timely basis, or at all, or if we are unable to successfully commercialize current and future indications of Auryxia or vadadustat on a timely basis, or at all, our business, financial condition and future profitability will be materially harmed.
- We have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses and cannot guarantee when, if ever, we will become profitable or attain positive cash flows.
- We will require substantial additional financing to achieve our goals. A failure to obtain this necessary capital when needed, or on acceptable terms, could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- Our independent registered public accounting firm has included an explanatory paragraph relating to our ability to continue as a going concern in its report on our audited financial statements included in this Annual Report on Form 10-K.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product and product candidates on unfavorable terms to us.
- We may not be successful in our efforts to identify, acquire, in-license, discover, develop and commercialize additional products or product candidates or our decisions to prioritize the development of certain product candidates over others may not be successful, which could impair our ability to grow.
- We may engage in strategic transactions to acquire assets, businesses, or rights to products, product candidates or technologies or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt, or cause us to incur significant expense.
- Our business has been and may continue to be, directly or indirectly, adversely affected by the COVID-19 pandemic.
- Our obligations in connection with the loan agreement with Pharmakon and requirements and restrictions in the loan agreement could adversely affect our financial condition and restrict our operations.
- Our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P. contains various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.
- If we are unable to maintain or expand sales and marketing capabilities or enter into additional agreements with third parties, we may not be successful in commercializing Auryxia, vadadustat, if approved, or any other product candidates that may be approved.
- Our, or our partners', failure to obtain or maintain adequate coverage, pricing and reimbursement for Auryxia, vadadustat, if approved, or any other future approved products could have a material adverse effect on our or our collaboration partners' ability to sell such approved products profitably and otherwise have a material adverse impact on our business.
- We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully than, we do.
- The commercialization of Riona and Vafseo™ in Japan and our current and potential future efforts with respect to the development and commercialization of our products and product candidates outside of the United States subject us to a variety of risks associated with international operations, which could materially adversely affect our business.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and commercialization of vadadustat and any other product candidates.
- We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.
- Conducting clinical trials outside of the United States makes us subject to additional risks and complexities and we may not complete such trials successfully, in a timely manner, or at all, which could affect our ability to obtain regulatory approvals.
- Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that may delay or prevent marketing approval or limit their commercial potential.
- We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat or any other product candidate, or we may experience significant delays in doing so, any of which would materially harm our business.
- Products approved for marketing are subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties, including withdrawal of marketing approval, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, when and if any of them is approved.

- We are subject to a complex regulatory scheme that requires significant resources to ensure compliance and our failure to comply with applicable laws could subject us to government scrutiny or enforcement, potentially resulting in costly investigations, fines, penalties or sanctions, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.
- We will incur significant liability if it is determined that we are promoting any "off-label" use of Auryxia or any other product we may develop, in-license or acquire or if it is determined that any of our activities violates the federal Anti-Kickback Statute.
- Legislative and regulatory healthcare reform may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain for any products that are approved in the United States or foreign jurisdictions.
- We depend on collaborations with third parties for the development and commercialization of Auryxia, Riona, Vafseo and vadadustat and if these collaborations are not successful or if our collaborators terminate their agreements with us, we may not be able to capitalize on the market potential of Auryxia, Riona, Vafseo and vadadustat, and our business could be materially harmed.
- We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.
- We rely on third parties to conduct all aspects of our product manufacturing and the loss of these manufacturers, their failure to supply us on a timely basis, or at all, or their failure to successfully carry out their contractual duties or comply with regulatory requirements, current good manufacturing practices requirements, or guidance could cause delays in or disruptions to our supply chain and substantially harm our business.
- We rely on third parties to conduct our clinical trials and certain of our preclinical studies. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain or maintain marketing approval for Auryxia, vadadustat or any of our product candidates, and our business could be substantially harmed.
- If the licensor of certain intellectual property relating to Auryxia terminates, modifies or threatens to terminate existing contracts or relationships with us, our business may be materially harmed.
- If we are unable to adequately protect our intellectual property, third parties may be able to use our intellectual property, which could adversely affect our ability to compete in the market.
- We may not be able to protect our intellectual property rights throughout the world.
- The intellectual property that we own or have licensed and related non-patent exclusivity relating to our current and future product candidates is, and may be, limited which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia.
- The market entry of one or more generic competitors or any third party's attempt to challenge our intellectual property rights will likely limit Auryxia sales and have an adverse impact on our business and results of operation.
- Litigation, including third party claims of intellectual property infringement, may be costly and time consuming and may delay or harm our drug discovery, development and commercialization efforts.
- We are currently involved in a declaratory judgment of non-infringement and invalidity lawsuit, opposition and invalidation proceedings, and may in the future be involved in additional lawsuits or administrative proceedings to challenge the patents of our competitors or to protect or enforce our patents, which could be expensive, time consuming, and unsuccessful.
- If we fail to attract, retain and motivate senior management and qualified personnel, we may be unable to successfully develop, obtain and/or maintain marketing approval of and commercialize vadadustat or commercialize Auryxia.
- We may encounter difficulties in managing our growth, including with respect to our employee base, and expanding our operations successfully.
- We have identified a material weakness in our internal control over financial reporting relating to our inventory process. If we are not able to remediate this material weakness, or if we experience additional material weaknesses or other deficiencies in the future or otherwise fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting which would harm our business and the trading price of our common stock.
- Our stock price has been and may continue to be volatile, which could result in substantial losses for holders or future purchasers of our common stock and lawsuits against us and our officers and directors.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company with the purpose of bettering the life of each person impacted by kidney disease. Since our initial public offering in 2014, we have built a business focused on developing and commercializing innovative therapeutics that we believe serves as a foundation for future growth. We have established ourselves as a leader in the kidney community, and we remain committed to helping patients and others where we believe our current and potential future products have the ability to deliver value. We believe that delivering value broadly to the kidney community, as well as others who may benefit from our medicines, will result in delivering value for shareholders. Our current portfolio includes a late-stage product candidate and a commercial product:

- ***Vadadustat*** is an investigational oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, or HIF, which stimulates erythropoietin, or EPO, production and leads to red blood cell, or RBC, production and improved oxygen delivery to tissues. The significance of the HIF pathway was recognized by the 2019 Nobel Prize and the 2016 Albert Lasker Basic Medical Research Award, which honored the three physician-scientists who discovered the HIF pathway and elucidated this primary oxygen sensing mechanism that is essential for survival. We believe that, based on the HIF-PH inhibitor mechanism of action and the results of our Phase 3 clinical trials, vadadustat has the potential to become the new oral standard of care for the treatment of anemia due to chronic kidney disease, or CKD.

  We completed the global Phase 3 clinical development program for vadadustat in September 2020 to support regulatory filings in the United States, Europe and other countries, which included two separate programs, INNO$_2$VATE and PRO$_2$TECT. INNO$_2$VATE evaluated vadadustat for the treatment of anemia due to CKD in adult patients on dialysis, or DD-CKD, and PRO$_2$TECT evaluated vadadustat for the treatment of anemia due to CKD in adult patients not on dialysis, or NDD-CKD.

  In May of 2020, we announced positive top-line results from our Phase 3 INNO$_2$VATE program that showed vadadustat was non-inferior to darbepoetin alfa, an injectable erythropoiesis-stimulating agent, or ESA, with respect to hematological efficacy (change in hemoglobin concentration) and cardiovascular safety (assessed in a time to the first occurrence of a major adverse cardiovascular event, or MACE, analysis, which is the composite of all-cause mortality, nonfatal myocardial infarction, or a nonfatal stroke) in treating anemia due to CKD in DD-CKD adult patients. In addition to meeting the primary endpoints of the INNO$_2$VATE program, vadadustat met the key secondary hematological efficacy endpoint in each of the two studies in the program and also met the program's key secondary safety endpoints. The results of the INNO$_2$VATE program were presented at American Society of Nephrology, or ASN, in October of 2020 and published in the *New England Journal of Medicine* in April of 2021.

  In September of 2020, we announced top-line results from our Phase 3 PRO$_2$TECT program that showed vadadustat was non-inferior to darbepoetin alfa with respect to hematological efficacy in treating anemia due to CKD in NDD-CKD adult patients. While the PRO$_2$TECT data showed that vadadustat achieved both the primary and key secondary hematological efficacy endpoints, it did not meet the program's primary cardiovascular safety (MACE) endpoint. These cardiovascular outcomes contrast with those reported within the INNO$_2$VATE program, which evaluated vadadustat for the treatment of anemia due to CKD in DD-CKD adult patients. The results of the PRO$_2$TECT program were presented at ASN in October of 2020 and published in the *New England Journal of Medicine* in April of 2021.

  We submitted a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, for vadadustat in March of 2021 for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. Our NDA submission was accepted for filing by the FDA in May of 2021 and the FDA has indicated that they are not currently planning to hold an Advisory Committee meeting to discuss the NDA for vadadustat. The FDA also assigned the application standard review and a Prescription Drug User Fee Act, or PDUFA, target action date of March 29, 2022. Our collaboration partner, Otsuka Pharmaceutical Co. Ltd., or Otsuka, submitted a Marketing Authorization Application, or MAA, for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients to the European Medicines Agency, or EMA, in October 2021. As vadadustat did not meet the PRO$_2$TECT program's primary safety endpoint, we are remaining cautious in our outlook for potential approval of vadadustat in NDD-CKD adult patients in the United States and Europe.

In June of 2020, we announced the first regulatory approval of vadadustat for the treatment of anemia due to CKD in DD-CKD and NDD-CKD adult patients in Japan. Our collaboration partner in Japan, Mitsubishi Tanabe Pharma Corporation, or MTPC, commenced commercial sales of vadadustat in Japan under the trade name, Vafseo™, in August 2020. In addition, MTPC filed a new drug application for vadadustat for the treatment of anemia due to CKD in adult patients in Taiwan in January of 2022.

In addition to anemia due to CKD, we believe that vadadustat has the potential to treat other serious or life-threatening conditions, including preventing and lessening the severity of acute respiratory distress syndrome, or ARDS, a complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, infection. More specifically, in July of 2020, we announced an investigator-sponsored clinical study by The University of Texas Health Science Center at Houston, or UTHealth, in Houston, Texas, evaluating the use of vadadustat as a potential therapy to prevent and lessen the severity of ARDS adult patients who have been hospitalized due to COVID-19. With the support of its data monitoring committee, UTHealth decided to expand the study beyond the initial 400 patients, an enrollment target they have now surpassed. Within this randomized, double-blind, placebo-controlled study, patients will be dosed with vadadustat or a placebo starting within 24 hours of hospital admission and continuing for up to 14 days. This study is being conducted under an Investigational New Drug application, or IND, with UTHealth as the study sponsor and is currently enrolling patients. In January of 2021, UTHealth announced that it had been awarded $5.1 million in funding from the U.S. Department of Defense, or DOD, to expand this clinical trial at its facilities.

- ***Auryxia*® *(ferric citrate)*** is approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with DD-CKD, or the Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with NDD-CKD, or the IDA Indication. Ferric citrate is also approved and marketed in Japan as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and for the treatment of patients with IDA, under the trade name Riona (ferric citrate hydrate). Since 2018, Auryxia product revenue has grown at a compounded annual growth rate of 14% due to market share gains and improved net price per pill, while total prescriptions for phosphate binders in the United States have declined 8%. We believe this growth is due to the benefits of the product perceived by the prescribing nephrologists as communicated by our nephrology-focused commercial and medical organizations.

If we obtain FDA approval of vadadustat, we plan to commercialize vadadustat in the United States with our well-established, nephrology-focused commercial organization, while also leveraging our collaboration with Otsuka and its U.S. nephrology commercial organization. In addition, in February 2022, we entered into a Second Amended and Restated License Agreement, or the Vifor Second Amended Agreement with Vifor (International) Ltd., or Vifor Pharma, which amended and restated the Amended and Restated License Agreement, dated April 8, 2019, or the Vifor First Amended Agreement. Pursuant to the Vifor Second Amended Agreement, we granted Vifor Pharma an exclusive license to sell vadadustat to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by us, to independent dialysis organizations that are members of group purchase organizations, and to certain non-retail specialty pharmacies in the United States, or the Territory. We refer to Fresenius Medical Care North America and its affiliates, these organizations and specialty pharmacies collectively as the “Supply Group". We currently retain rights to commercialize vadadustat for use in the non-dialysis dependent CKD market and to sell to dialysis organizations outside of the Supply Group. During the term of the Vifor Second Amended Agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the Territory to the Supply Group.

We market Auryxia in the United States with our well-established, nephrology-focused commercial organization. Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona in Japan.

In addition, we continue to explore additional development opportunities to expand our pipeline and portfolio of novel therapeutics through both internal research and external innovation. Our development pipeline includes several earlier stage opportunities, including praliciguat, an investigational oral soluble guanylate cyclase, or sGC, stimulator, that we licensed from Cyclerion Therapeutics, Inc., or Cyclerion, in June 2021. Praliciguat is in development for the treatment of focal segmental glomerulosclerosis, which is highly complementary to our strategy to identify and develop novel therapeutics for people impacted by kidney diseases.

Further, our internal innovation efforts include several preclinical opportunities, both in the HIF pathway, leveraging our learnings from the research and development of vadadustat, as well as new areas of focus we are currently exploring.

Strategy

Our mission and our culture are centered around the goal of improving the lives of people impacted by kidney disease through the discovery, development and commercialization of innovative therapeutics. Our strategy is to execute on the following initiatives, which we believe will create significant market opportunities for us:

- ***Prepare for the potential commercialization of vadadustat for the treatment of anemia due to CKD in the United States.*** We believe vadadustat has the potential to address limitations of injectable ESAs, and become the new oral standard of care for the treatment of anemia due to CKD, if approved. We submitted an NDA to the FDA for vadadustat in March of 2021, which was accepted by the FDA in May of 2021. The FDA assigned the application standard review and a PDUFA target action date of March 29, 2022. We believe we are well positioned to commercialize vadadustat in the United States with our nephrology-focused commercial team, our partnership with Otsuka, and the Vifor Second Amended Agreement, if vadadustat receives FDA approval.
- ***Support vadadustat adoption and growth outside of the United States.*** We plan to continue to support MTPC's commercialization and growth of Vafseo in Japan. In addition, Otsuka submitted a MAA for vadadustat to the EMA in October 2021, and MTPC filed a new drug application for vadadustat for the treatment of anemia due to CKD in adult patients in Taiwan in January 2022. We also plan to support MTPC's and Otsuka's commercialization efforts for vadadustat in Japan and Europe and certain other markets for which MTPC and Otsuka have commercialization rights, subject to the applicable regulatory approvals. We retain full commercial rights to vadadustat in Latin America, allowing us maximum flexibility in the region.
- ***Maximize the value of Auryxia, and leverage the product as a commercial foundation for vadadustat, in CKD.*** We aim to continue to use our nephrology-focused commercial organization to increase awareness, demand for and adoption of Auryxia for its approved indications with key stakeholders including nephrologists, third-party payors, dialysis organizations, patients and their families. In addition to bringing meaningful clinical benefits to patients, Auryxia provides strategic value to Akebia by allowing us to leverage our existing nephrology-focused commercial footprint and deepen key customer and prescriber relationships that we believe will be important for the future commercialization of vadadustat, if approved, and other potential future renal products.
- ***Advance vadadustat clinical development for additional therapeutic indications.*** In addition to our CKD program and the ARDS study, we plan to identify and initiate development planning for other programs where vadadustat may have therapeutic benefits.
- ***Continue to expand our pipeline and portfolio of novel therapeutics.*** We aim to continue to add to our pipeline and portfolio of novel therapeutics through internal research, discovery and development, and through external innovation and strategic transactions, such as in-licenses, collaborations and acquisitions. In June 2021, we entered into the Cyclerion Agreement with Cyclerion, pursuant to which Cyclerion granted us an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral sGC stimulator, which is highly complementary to our strategy to identify and develop novel therapeutics for people impacted by kidney disease. We plan to continue to develop praliciguat and explore similar opportunities that align with our strategic vision in the future. In addition, given our expertise in research and development, we believe there may be opportunities to leverage these assets and establish mutually beneficial relationships with other companies that are looking to enter the renal market or attempting to develop renal therapeutics.

Our management team has extensive experience in developing and commercializing drugs for the treatment of renal and metabolic disorders, a deep understanding of the renal space and biological pathways involved in kidney disease including HIF biology and iron metabolism, and broad business development expertise. We believe we are well positioned to execute on our strategy.

Background on Kidney Disease

Kidney disease is an area of major unmet need globally, driving massive healthcare costs and with a generally poor prognosis: eventually many patients will progress to a stage where they are dependent on dialysis, with high morbidity and a significant increase in mortality rate.

Kidney disease can be caused by a number of distinct and concomitant factors, including cardiometabolic disorders (primarily diabetes and hypertension), genetic diseases, autoimmune disorders, and aging. Given the prevalence and growth rates of these various underlying conditions, kidney disease prevalence is expected to continue to increase globally. In the United States, CKD significantly impacts the U.S. healthcare system, potentially affecting about 37 million patients and costing Medicare nearly $120 billion annually for treating Medicare beneficiaries with CKD of end-stage renal disease or end-stage kidney disease, or ESRD or ESKD, according to the Centers for Disease Control and Prevention. The U.S. Department of Health and

Human Services has recognized this national pandemic and partnered with ASN to found the KidneyX Innovation Accelerator, a public-private partnership to improve the lives of the 850 million people worldwide currently affected by kidney diseases by accelerating innovation in the prevention, diagnosis and treatment of kidney diseases.

Most of the conditions covered by the term “kidney disease” may lead to renal failure and dependence on dialysis or kidney transplant for survival. Dependence on dialysis is associated with a significant increase in mortality and hospitalizations, and a significant reduction in quality of life for patients. There is a clear need to improve the clinical and quality of life outcomes for people living with kidney disease. We are driven by our purpose, to provide or contribute to better alternatives that improve the lives of people impacted by kidney disease.

CKD is a condition in which the kidneys are progressively damaged to the point that they cannot properly filter the blood circulating in the body. This damage causes waste products to build up in the patient’s blood leading to other health problems, including anemia, cardiovascular disease and bone disease. As illustrated in the table below, CKD patients are categorized in one of five stages based on the degree of their loss of kidney function as measured by the glomerular filtration rate, or GFR, and the level of protein in the urine, referred to as albuminuria.

Stages and Prevalence of CKD in the United States

Stage	Description	GFR (mL/min/1.73m2) a	U.S. Prevalence Rates b, c	Estimated Number of U.S. Patients (millions) d, e
1	Kidney damage with normal or increased GFR	≥90	4.6%	11.2
2	Kidney damage with mildly decreased GFR	60-89	3.0%	7.3
3	Moderately decreased GFR	30-59	6.7%	16.4
4	Severely decreased GFR	15-29	0.4%	1.0
5	Kidney failure (includes non dialysis, dialysis and transplant)	<15 (or dialysis)	0.3% (calculated)	0.7

Sources:

a. GFR categories defined in the August 2012 Kidney Disease Improving Global Outcomes Clinical Practice Guideline for Anemia in Chronic Kidney Disease, p. vii.

b. U.S. Prevalence Rates for Stages 1-4 based on averages of data from 2011-2012, 2013-2014, and 2015-2016, CDC CKD Surveillance System, National Health and Nutrition Examination Survey.

c. U.S. Prevalence Rate for Stage 5 is based on a calculation using estimated number of U.S. patients with ESRD from 2018 U.S. Renal Data System Annual Report, February 21, 2019, as set forth in this table, and U.S. population data for people 20 years and older from www.census.gov.

d. Estimated Number of U.S. Patients for Stages 1-4 based on the 2018 U.S. Prevalence rates, as set forth in this table, as applied by Akebia to U.S. population data for people 20 years and older from www.census.gov.

e. Estimated Number of U.S. End-Stage Renal Disease Patients from 2018 U.S. Renal Data System Annual Report, February 21, 2019.

The prevalence and incidence of CKD is increasing in all segments of the United States population. Risk factors for the development of CKD include concomitant diseases such as hypertension, diabetes mellitus and cardiovascular disease, lifestyle factors such as tobacco use and inactivity, family history, aging and prenatal factors such as maternal diabetes mellitus, low birth weight and small-for-gestational-age status.

The progression of CKD towards renal failure is complicated by multiple conditions which further deteriorate kidney function and the general health of patients if left untreated. Typically the prevalence of these conditions increases as CKD progresses. For instance, anemia is characterized by low hemoglobin levels and is typically associated with a worsening quality of life, increased hospitalizations and increased mortality. The prevalence of anemia increases with the severity of CKD from an estimated 20% in patients with Stage 3 NDD-CKD to an estimated 95% in patients with Stage 5 DD-CKD.

Anemia, or low hemoglobin/red blood count, in patients with CKD most commonly arises from two etiologies:

1. Anemia due to CKD: results from inadequate levels of EPO, a protein hormone synthesized by specialized cells in the kidney that stimulates RBC production in the bone marrow. As renal function declines, the body progressively loses the ability to produce endogenous EPO; and
2. IDA: results from low levels of iron due to abnormal iron absorption and utilization in patients with CKD.

The global Phase 3 clinical development program for vadadustat evaluated the efficacy and safety of vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. We submitted an NDA to the FDA, for vadadustat in March of 2021 for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients.

IDA in adult patients with NDD-CKD is an FDA-approved indication for Auryxia. Hyperphosphatemia in DD-CKD patients is also an FDA-approved indication for Auryxia. Hyperphosphatemia is another condition associated with CKD that is characterized by elevated serum phosphorus levels and is also typically associated with a worsening of health including increased cardiovascular risk and mortality.

Vadadustat

Market Opportunity for Vadadustat

Anemia due to Chronic Kidney Disease

Anemia is common in patients with CKD, and its prevalence increases with disease progression. Anemia due to CKD results from inadequate EPO levels, which negatively affect RBC production. Left untreated, anemia accelerates overall deterioration of patient health with increased morbidity and mortality. Based on third party prevalence data and company estimates, potentially 37 million people in the United States have CKD and approximately 5.7 million of these individuals suffer from anemia. The current standard of care for anemia due to CKD is treatment by injectable recombinant human ESAs, such as Epogen® (epoetin alfa), Aranesp® (darbepoetin alfa) and Mircera® (methoxy polyethylene glycol-epoetin beta), or blood transfusion. Based on publicly available information on ESA sales and market data compiled by a third-party vendor, global sales of injectable ESAs for all uses were estimated to be approximately $6.1 billion in 2018. The vast majority of these sales are believed to have been for the treatment of anemia due to CKD.

When administered to a patient, injectable ESAs provide supraphysiological levels of exogenous EPO to stimulate production of RBCs. While injectable ESAs can be effective in raising hemoglobin levels, they have the potential to cause significant side effects, and need to be injected subcutaneously or intravenously. In particular, injectable ESAs may lead to thrombosis, stroke, myocardial infarction and death. Also, several randomized clinical trials have demonstrated that higher hemoglobin targets
(≥13.0 g/dL) with ESA use are associated with increased cardiovascular risk, leading to changes in regulatory and clinical practice guidance. While these safety concerns, which became evident starting in 2006, have led to a significant reduction in the use of injectable ESAs, and an increase in the use of injectable iron, injectable ESAs remain the current standard of care for both DD-CKD and NDD-CKD patients with anemia.

DD-CKD Market

We believe there is a significant opportunity for vadadustat to address limitations of injectable ESAs and become the new oral standard of care for the treatment of anemia due to CKD in DD-CKD adult patients, if approved. In addition to clinical data from our Phase 3 INNO$_2$VATE program that showed vadadustat was non-inferior to darbepoetin alfa with respect to hematological efficacy (change in hemoglobin concentration) and cardiovascular safety (MACE) in DD-CKD adult patients, we believe the potential opportunity for vadadustat within the DD-CKD market is supported by a number of factors including vadadustat's convenient oral dosing and unique U.S. dialysis market dynamics.

According to the U.S. Renal Data System, or USRDS, 2020 Annual Data Report, there were approximately 556,000 patients in the United States on dialysis in 2018, of which 88% were on in-center hemodialysis and the remainder on home dialysis, which includes both peritoneal dialysis and home hemodialysis. Injectable ESAs are administered by dialysis center staff to approximately 90% of in-center hemodialysis patients and 75% of home dialysis patients. Although the significant majority of dialysis patients are cared for in-center, recently, several factors including the COVID-19 pandemic, changing patient preferences, government initiatives, and reimbursement changes are supporting a shift toward home dialysis. We believe as an oral therapeutic, vadadustat has potential to be a convenient treatment alternative to injectable ESAs not only for in-center dialysis patients, but also for the growing number of home dialysis patients and patients transitioning to home dialysis.

Given the concentration of dialysis clinics in large networks, with DaVita, Inc., or DaVita, and Fresenius Kidney Care Group accounting for a vast majority of the dialysis population in the United States, treatment is usually driven by medical protocols that are implemented across the entire network of clinics. These protocols are informed by very large data sets and when

updated, result in rapid change applicable to large segments of the patient population. This is particularly true of medications covered under the End Stage Renal Disease, or ESRD, Prospective Payment System, or PPS, in Medicare, or the ESRD Bundle, a payment structure with a flat base rate per dialysis session adjusted for individual patient and facility characteristics. Dialysis-related drugs are included in the ESRD Bundle if they fall into functional categories such as anemia management and bone and mineral metabolism, except that oral-only drugs are exempted from inclusion until 2025. In a final ESRD PPS rule published in November 2018, CMS confirmed that it will expand the Transitional Drug Add-on Payment Adjustment, or TDAPA, to all new dialysis drugs approved by the FDA after January 1, 2020. The TDAPA will provide separate payment for new drugs for two years based on the drug's Average Sales Price, or ASP, that will be in addition to the base rate in order to facilitate the adoption of innovative therapies. Although there are several details that need further clarification, and the precise timing of when we could receive codes to allow for reimbursement under TDAPA is not known, the codes are assigned on a quarterly basis, and the rule provides support for our assumption that new anemia treatments, including those in the HIF-PH inhibitor class, will be included in the ESRD Bundle and will be eligible for separate payment initially under TDAPA.

NDD-CKD Market

Data from the USRDS 2015 Annual Data Report indicate that the collective injectable ESA treatment rate in NDD-CKD patients in the United States decreased by approximately half from 2009 to 2013 as a result of the safety concerns associated with ESAs. Today, a high proportion of NDD-CKD patients with anemia are either not treated or inadequately treated despite having low hemoglobin levels. In contrast to treatment with ESAs, we believe vadadustat, if approved for use in NDD-CKD patients, has the potential to expand the number of NDD-CKD patients receiving treatment by offering an alternative oral treatment for anemia due to CKD.

Results from our Phase 3 PRO_2TECT program showed vadadustat was non-inferior to darbepoetin alfa with respect to hematological efficacy in treating anemia due to CKD in NDD-CKD adult patients, meeting both the primary and key secondary hematological efficacy endpoints. However, it did not meet the program's primary cardiovascular safety (MACE) endpoint. We are pursuing regulatory approval for vadadustat for the treatment of anemia due to CKD in NDD-CKD adult patients; however, as PRO_2TECT did not meet the program's primary safety endpoint, we remain cautious in our outlook for potential approval of vadadustat as a treatment for anemia due to CKD in NDD-CKD adult patients.

Vadadustat Has the Potential to Become the New Oral Standard of Care

We believe vadadustat has the potential to become the new oral standard of care for the treatment of anemia due to CKD, if approved. Below is a summary of certain of the key clinical findings; further details are included in the discussion below.

- *Vadadustat stimulated endogenous EPO production.* In two Phase 1 studies in normal healthy volunteers and one Phase 2 study in CKD patients, vadadustat increased serum EPO levels in a dose-dependent manner. Pre-dose EPO levels returned to baseline levels prior to subsequent daily dose. In these studies, vadadustat stimulated endogenous EPO production while avoiding supraphysiologic EPO levels.
- *Vadadustat significantly increased and maintained hemoglobin levels.* Our global Phase 3 program and Phase 2 studies in CKD patients with anemia demonstrated that vadadustat significantly increased and/or maintained hemoglobin levels.
- *Vadadustat was dosed orally once daily and three times weekly.* Our Phase 2 studies showed that vadadustat can be orally dosed once daily in NDD-CKD patients with up to 20 weeks of dosing. This study also showed the potential for three-times weekly dosing of vadadustat in DD-CKD patients. We are conducting additional larger studies of vadadustat evaluating three-times weekly dosing and a modified approach to once-daily dosing.

Based on this and other data, we believe vadadustat has the potential to be a treatment for anemia due to CKD and become the new oral standard of care by:

- stimulating erythropoiesis and avoiding supraphysiologic EPO levels;
- increasing hemoglobin in a predictable and controlled manner;
- minimizing hemoglobin excursions; and
- providing convenient oral dosing.

Vadadustat Clinical Development Program

Below is a summary of the clinical development work undertaken for vadadustat.

Vadadustat Global Phase 3 Clinical Program in Anemia Due To CKD

We conducted a global Phase 3 clinical development program for vadadustat, which included two programs, INNO$_2$VATE and PRO$_2$TECT. INNO$_2$VATE evaluated vadadustat in adult DD-CKD patients with anemia due to CKD in two studies, and PRO$_2$TECT evaluated vadadustat in adult NDD-CKD patients with anemia due to CKD in two studies. Combined, we enrolled approximately 7,500 patients in these studies and evaluated once daily oral dosing of vadadustat against an injectable ESA active comparator, darbepoetin alfa.

Both the INNO$_2$VATE and PRO$_2$TECT Phase 3 programs were global, multicenter, open-label, sponsor-blind, active-controlled non-inferiority programs. In both programs, patients were randomized 1:1 to receive either oral vadadustat or injectable darbepoetin alfa. The primary efficacy endpoint for each study in the INNO$_2$VATE and PRO$_2$TECT programs was the mean change in hemoglobin between baseline and the primary evaluation period. Non-inferiority, or NI, for the primary efficacy endpoint was achieved if the lower bound of the 95% confidence interval for the between-group difference of the mean hemoglobin change did not fall below the pre-specified NI margin. Both the INNO$_2$VATE and PRO$_2$TECT programs included the primary safety endpoint of the assessment of MACE, with a comparison of vadadustat to darbepoetin alfa. MACE is defined as the composite endpoint of all-cause mortality, non-fatal myocardial infarction, or non-fatal stroke. The primary safety analysis for each program was based on the combined MACE events from the two studies in each of INNO$_2$VATE and PRO$_2$TECT. NI for the primary safety analysis was achieved if the upper bound of the 95% confidence interval for the hazard ratio of vadadustat to darbepoetin alfa did not exceed the pre-specified NI margin. We prospectively defined and agreed to non-inferiority margins with the United States and European regulatory authorities and agreed with the United States regulatory authorities on the key components of our statistical analysis plan.

Top-line Results from Global Phase 3 INNO$_2$VATE Program within DD-CKD Adult Patients

The two INNO$_2$VATE studies (*Correction/Conversion* and *Conversion*), which collectively enrolled 3,923 patients, evaluated the efficacy and safety of vadadustat versus darbepoetin alfa for the treatment of anemia due to CKD in DD-CKD adult patients.

Vadadustat achieved the primary and key secondary efficacy endpoint in each of the two INNO$_2$VATE studies, demonstrating non-inferiority to darbepoetin alfa as measured by a mean change in hemoglobin, or Hb, between baseline and the primary evaluation period (weeks 24 to 36) and secondary evaluation period (weeks 40 to 52). Vadadustat also achieved the primary safety endpoint of the INNO$_2$VATE program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE across both INNO$_2$VATE studies.

Primary and Key Secondary Efficacy Endpoint Results

Vadadustat achieved each of the INNO$_2$VATE studies' primary efficacy endpoints of mean change in Hb between baseline and the primary evaluation period compared to darbepoetin alfa, in DD-CKD adult patients, demonstrating non-inferiority to darbepoetin alfa based on using a non-inferiority margin of -0.75 g/dL.

In INNO$_2$VATE's *Correction/Conversion* study of incident dialysis patients (n=369):

- ***Primary Efficacy Endpoint Result***: Vadadustat was *non-inferior* to darbepoetin alfa. The least square mean difference in Hb was -0.31 g/dL (95% CI: -0.53, -0.10), achieving the pre-specified non-inferiority criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.36 (1.13) g/dL for vadadustat-treated patients compared to 10.61 (0.94) g/dL for darbepoetin alfa-treated patients.
- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained the target Hb efficacy response at weeks 40 to 52 achieving non-inferiority compared to darbepoetin alfa. The least square mean difference in Hb was -0.07 g/dL (95% CI: -0.34, 0.19). The mean (SD) Hb level at week 40 to week 52 was 10.51 (1.19) g/dL for vadadustat treated-patients compared to 10.55 (1.14) g/dL for darbepoetin alfa-treated patients.

In INNO$_2$VATE's *Conversion* study of prevalent dialysis patients (n=3,554):

- ***Primary Efficacy Endpoint Result***: Vadadustat was *non-inferior* to darbepoetin alfa. The least square mean difference in Hb was -0.17 g/dL (95% CI: -0.23, -0.10), achieving the pre-specified non-inferiority criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.36 (1.01) g/dL for vadadustat-treated patients compared to 10.53 (0.96) g/dL for darbepoetin alfa-treated patients.
- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained efficacy in the *Conversion* study demonstrating non-inferiority to darbepoetin with a least square mean difference in Hb of -0.18 g/dL (95% CI: -0.25, -0.12). The mean (SD) Hb level at week 40 to week 52 was 10.40 (1.04) g/dL in the vadadustat-treated patients compared to 10.58 (0.98) g/dL for darbepoetin treated patients.

Primary Safety Major Adverse Cardiovascular Events (MACE) Endpoint Result

Vadadustat achieved the INNO$_2$VATE program's primary safety endpoint of non-inferiority for MACE. In the primary analysis of time to first MACE event, vadadustat demonstrated non-inferiority to darbepoetin alfa using a non-inferiority margin of 1.25 based on discussion with the FDA and a non-inferiority margin of 1.3 based on discussion with the EMA.

The INNO$_2$VATE program (*Correction/Conversion* and *Conversion* studies) of dialysis patients (n=3,902):

- Vadadustat was *non-inferior* to darbepoetin alfa. The upper bound of the 95% confidence interval (CI) of the Hazard Ratio (HR) was below the pre-specified non-inferiority margin of 1.25 for primary MACE analysis (HR 0.96, 95% CI: 0.83, 1.11.).

The incidence of treatment emergent adverse events during the *Correction/Conversion* study in vadadustat treated patients was 83.8% and 85.5 % in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were hypertension (16.2%/ 12.9%) and diarrhea (10.1%/ 9.7%). Serious treatment emergent adverse events were lower in vadadustat treated patients at 49.7% compared to 56.5% for darbepoetin alfa treated patients. The incidence of treatment emergent adverse events during the *Conversion* study in the vadadustat treated patients was 88.3%, and 89.3% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were diarrhea (13.0%/ 10.1%), pneumonia (11.0%/ 9.7%), hypertension (10.6%/ 13.8%), and hyperkalemia (9.0%/ 10.8%). Serious treatment emergent adverse events were slightly lower for vadadustat treated patients at 55.0% and 58.3% for darbepoetin alfa-treated patients. Patients with DD-CKD experienced an increased risk of thromboembolic events compared to darbepoetin alfa with a time to first event HR of 1.20 (95% CI 0.96 - 1.50) driven by thrombosis of vascular access.

INNO$_2$VATE results on key secondary safety endpoints showed that vadadustat also demonstrated non-inferiority to darbepoetin alfa in analyses of expanded MACE, cardiovascular MACE, cardiovascular mortality, and all-cause mortality.

Top-line Results from Global Phase 3 PRO$_2$TECT Program within NDD-CKD Adult Patients

The two PRO$_2$TECT studies (*Correction* and *Conversion*), which collectively enrolled 3,476 patients, evaluated the efficacy and safety of vadadustat for the treatment of anemia due to CKD in NDD-CKD adult patients.

Vadadustat achieved the primary and key secondary efficacy endpoint in each of the two PRO$_2$TECT studies, demonstrating non-inferiority to darbepoetin alfa as measured by a mean change in Hb between baseline and the primary evaluation period (weeks 24 to 36) and secondary evaluation period (weeks 40 to 52). Vadadustat did not meet the primary safety endpoint of the PRO$_2$TECT program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE, across both PRO$_2$TECT studies.

Primary and Key Secondary Efficacy Endpoint Results

Vadadustat achieved each of the PRO$_2$TECT studies' primary efficacy endpoints of mean change in Hb between baseline and the primary evaluation period compared to darbepoetin alfa, in adult patients on dialysis, demonstrating non-inferiority to darbepoetin alfa using an NI margin of -0.75 g/dL.

In PRO$_2$TECT's *Correction* study (n=1,751):

- ***Primary Efficacy Endpoint Result***: Vadadustat was non-inferior to darbepoetin alfa. The least square mean difference in Hb was 0.05 g/dL (95% CI: -0.04, 0.15), achieving the pre-specified NI criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.39 (0.99) g/dL for vadadustat-treated patients compared to 10.35 (1.03) g/dL for darbepoetin alfa-treated patients.
- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained the target Hb efficacy response at weeks 40 to 52 achieving non-inferiority compared to darbepoetin alfa. The least square mean difference in Hb was 0.04 g/dL (95% CI: -0.06, 0.14). The mean (SD) Hb level at week 40 to week 52 was 10.48 (1.05) g/dL for vadadustat-treated patients compared to 10.45 (1.01) g/dL for darbepoetin alfa-treated patients.

In PRO$_2$TECT's *Conversion* study (n=1,725):

- ***Primary Efficacy Endpoint Result***: Vadadustat was non-inferior to darbepoetin alfa. The least square mean difference in Hb was -0.01 g/dL (95% CI: -0.09, 0.07), achieving the pre-specified NI criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.77 (0.98) g/dL for vadadustat-treated patients compared to 10.77 (0.99) g/dL for darbepoetin alfa-treated patients.

- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained efficacy in the *Conversion* study demonstrating non-inferiority to darbepoetin with a least square mean difference in Hb of 0.00 g/dL (95% CI: -0.10, 0.09). The mean (SD) Hb level at week 40 to week 52 was 10.80 (1.04) g/dL in the vadadustat-treated patients compared to 10.79 (1.05) g/dL for darbepoetin alpha-treated patients.

Primary Safety Major Adverse Cardiovascular Events (MACE) Endpoint Result

The PRO_2TECT program (*Correction* and *Conversion* studies) (n=3,471):

- ***Primary Safety MACE Endpoint Result***: Vadadustat did not meet the PRO_2TECT program's primary safety endpoint of non-inferiority for MACE. The upper bound of the 95% confidence interval of the Hazard Ratio (HR) was above the pre-specified NI margin of 1.25 for primary MACE analysis (HR 1.17, 95% CI: 1.01, 1.36).

Analysis of MACE events conducted by Akebia in the PRO_2TECT program revealed that the greater number of MACE events observed among vadadustat patients as compared to the active comparator was primarily related to an excess of non-cardiovascular death and death-of-unknown-cause in regions outside of the United States where significant differences in treatment patterns for NDD-CKD patients were observed.

The PRO_2TECT analysis plan was prospectively designed to analyze the effect of regional differences, most notably, well-known differences in Hb treatment targets. Within PRO_2TECT, U.S. patients were treated to a target Hb range of 10 to 11 g/dL and non-U.S. patients were treated to a target Hb range of 10 to 12 g/dL. In October of 2020, we presented a pre-specified regional analysis that showed vadadustat was not associated with a clinically meaningful increase in cardiovascular risk compared to darbepoetin alfa in U.S. patients treated to a target Hb range of 10 to 11 g/dL, in an analysis of MACE (HR 1.06, 95% CI: 0.87, 1.29).

In March 2021, based on these analyses and the totality of the data from our Phase 3 program, we submitted an NDA to the FDA for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. However, as vadadustat did not meet the PRO_2TECT program's primary safety endpoint, we remain cautious in our outlook for potential approval of vadadustat in adult NDD-CKD patients.

The incidence of treatment emergent adverse events during the *Correction* study in the vadadustat-treated patients was 90.9%, and 91.6% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (34.7%/ 35.2%), hypertension (17.7%/ 22.1.%), hyperkalemia (12.3.%/ 15.6%), urinary tract infection (12.9%/ 12.0%), diarrhea (13.9%/ 10.0%), peripheral oedema (12.5%/ 10.5%), fall (9.6%/ 10%) and nausea (10%/ 8.2%). Serious treatment emergent adverse events were 65.3% for vadadustat-treated patients and 64.5% for darbepoetin alfa-treated patients. The incidence of treatment emergent adverse events during the *Conversion* study in vadadustat treated patients was 89.1% and 87.7% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (27.5%/ 28.4%), hypertension (14.4%/ 14.8%), urinary tract infection (12.2%/ 14.5%), diarrhea (13.8.%/ 8.8.%), peripheral oedema (9.9%/ 10.1%) and pneumonia (10.0%/ 9.7%). Serious treatment emergent adverse events were 58.5% for vadadustat-treated patients and 56.6% for darbepoetin alfa-treated patients.

We are also conducting additional studies of vadadustat evaluating a modified approach to once-daily and three-times weekly dosing, including assessment of a vadadustat starting dose based on an individual’s pre-conversion ESA dose prior to study entry and higher titration doses of vadadustat (up to 1200 mg). We believe data from these and other studies could support registration of the modified approach to once daily dosing and three times weekly dosing, and further strengthen our potential commercial position if vadadustat is approved for marketing.

Hepatic Safety Profile of Vadadustat in Clinical Studies

Following the completion of our global Phase 3 clinical program for vadadustat, there was a review of hepatic safety across the vadadustat clinical program, which includes 8 completed Phase 2 and 3 studies in NDD-CKD patients, 10 completed Phase 1, 2, and 3 studies, and one ongoing Phase 3b study in patients with DD-CKD, and 18 completed studies in healthy subjects (17 Phase 1 and one Phase 3). This review included a blinded assessment of all hepatic events in the studies by a panel of hepatic experts and analysis by an independent hepatic expert and our team. Hepatocellular injury attributed to vadadustat was reported in less than 1% of patients; there was one case of severe hepatocellular injury with jaundice. All events were asymptomatic and resolved after discontinuation of vadadustat.

Commercialization

We are supporting MTPC's commercialization of vadadustat in Japan, preparing for a potential commercial launch of vadadustat in the United States and supporting potential commercial launches of vadadustat in certain other markets. Our ability to launch vadadustat in the United States is dependent on the successful review of the NDA, and approval by the FDA.

If we obtain FDA approval of vadadustat, we plan to commercialize vadadustat in the United States with our well-established, nephrology-focused commercial organization, while leveraging our collaboration with Otsuka and its U.S. nephrology commercial organization. We granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. Otsuka submitted a MAA for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients to the EMA in October 2021. We granted MTPC exclusive rights to commercialize vadadustat in Japan, where MTPC commenced commercial sales of vadadustat under the trade name, Vafseo™, in August 2020, and in certain other countries in Asia, subject to marketing approvals. In addition, MTPC filed a new drug application for vadadustat for the treatment of anemia due to CKD in adult patients in Taiwan.

In addition, in February 2022, we entered into the Vifor Second Amended Agreement with Vifor Pharma, which amended and restated the Vifor First Amended Agreement. Pursuant to the Vifor Second Amended Agreement, we granted Vifor Pharma an exclusive license to sell vadadustat to the Supply Group in the Territory. We currently retain rights to commercialize vadadustat for use in the non-dialysis dependent CKD market and to sell to dialysis organizations outside of the Supply Group. During the term of the Vifor Second Amended Agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the Territory to the Supply Group. For more information about our license, collaboration and strategic agreements relating to vadadustat, see Part I, Item 1. Business – License, Collaboration and Other Strategic Agreements – Vadadustat.

In February 2020, the Company entered into a letter agreement, or the Letter Agreement, with Vifor Pharma relating to Vifor Pharma's agreement with a third party to purchase a Priority Review Voucher, or the PRV, issued by the FDA, or the PRV Purchase. A PRV entitles the holder to priority review of an NDA, or a Biologics License Application for a new drug, which reduces the target FDA review time to six months after official acceptance of the submission, and could lead to expedited approval. Pursuant to the Letter Agreement, we paid Vifor Pharma $10.0 million in connection with the closing of the PRV Purchase. In March of 2021, we submitted an NDA for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. Our NDA submission did not include a PRV. In August 2021, we entered into an amendment to the Letter Agreement with Vifor Pharma whereby the parties agreed that Vifor Pharma would sell the PRV to a third party, and we and Vifor Pharma will share the proceeds from the sale based on certain terms. In the fourth quarter of 2021, Vifor Pharma sold the PRV to a third party, and Vifor Pharma paid us $8.6 million in proceeds from the sale. These proceeds were subsequently paid to Otsuka as reimbursement for their contribution to the purchase of the PRV, as required under a separate Letter Agreement executed with Otsuka.

Our Commercial Product: Auryxia

Auryxia (ferric citrate) is a non-calcium, non-chewable, orally-administered tablet that was approved for marketing by the FDA in September 2014 as a phosphate binder for the Hyperphosphatemia Indication and was commercially launched in the United States shortly thereafter. In November 2017, Auryxia received marketing approval from the FDA for a second indication, the IDA Indication, and was commercially launched for this indication in the United States shortly thereafter.

In January 2014, our Japanese sublicensee, JT, received approval from the Japanese Ministry of Health, Labour and Welfare to market ferric citrate hydrate in Japan under the trade name Riona as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and was commercially launched in Japan shortly thereafter. In July 2019, JT, and its subsidiary, Torii, reported positive top-line results from a pivotal Phase 3 comparative study evaluating Riona for the treatment of IDA in adult patients in Japan. In May 2020, JT and Torii filed an application for approval of IDA as an additional indication for Riona in Japan, which was approved in March 2021.

In September 2015, we received approval to market ferric citrate in the European Union under the tradename Fexeric. Pursuant to the sunset clause under EU law, the European Commission's approval of Fexeric in the EU was contingent on, among other things, our commencing marketing of Fexeric within three years. Although we successfully negotiated an extension to December 23, 2019, we did not commence marketing Fexeric by such date and therefore the Fexeric approval in the EU has ceased to be valid.

We have licensed and sublicensed certain intellectual property rights covering Auryxia from Panion & BF Biotech, Inc., or Panion. For more information regarding our intellectual property rights to Auryxia and our license agreement with Panion see Part I, Item 1. Business – Intellectual Property – Auryxia and Part I, Item 1. Business - License, Collaboration and Other Strategic Agreements – License Agreement with Panion & BF Biotech, Inc. We received Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg iron per tablet), with the first received on October 31, 2018. We filed certain complaints for

patent infringement relating to such ANDAs, and have entered into settlement and license agreements with each of the ANDA filers. See Part I, Item 3. Legal Proceedings for further information relating to the ANDAs, lawsuits and settlements.

Market Opportunity

Hyperphosphatemia

Hyperphosphatemia is a metabolic disorder characterized by elevated serum phosphorus levels. Phosphorus is a vital element required for most cellular processes and, in individuals with normal kidney function, excess dietary phosphorus is removed by the kidneys and excreted in urine. In adults with functioning kidneys, normal serum phosphorus levels are 2.5 to 4.5 mg/dL. In adults with DD-CKD, elevated phosphorus levels, or hyperphosphatemia, can be associated with adverse effects, including increased risk for cardiovascular disease, bone disease and death.

Phosphate binders are the only interventions marketed for the treatment of hyperphosphatemia. According to the USRDS 2020 Annual Data Report, there were approximately 556,000 adult patients in the United States with DD-CKD in 2018, of which approximately 80% were treated with a phosphate binder. Phosphate binders need to be taken with meals and snacks, and it is not uncommon for DD-CKD patients to be prescribed as many as 12 or more phosphate binder pills per day, among other medications. Patients taking phosphate binders also experience gastrointestinal tolerability issues. As a result of the pill burden and tolerability issues associated phosphate binders, prescribed phosphate binders are often intolerable for many patients, leading to lack of treatment adherence and compliance.

In addition, in 2018 approximately 42% of patients treated with a phosphate binder were treated solely with a calcium-based binder, which can lead to side effects such as increased cardiovascular risk, hypercalcemia and gastrointestinal-related adverse events. Due to the risks associated with calcium-based binders, in 2017 Kidney Disease: Improving Global Outcomes, or KDIGO, recommended that clinicians limit the use of calcium-based binders.

Sevelamer and lanthanum-based phosphate binders are other alternatives. Lanthanum is a rare earth element and is minimally absorbed in the gastrointestinal tract. Lower level tissue deposition, particularly in bone and liver, has been observed in animals, however, the long-term, potentially harmful, effects due to the accumulation of lanthanum in these tissues have not been clearly determined.

Aluminum-type phosphate binders were widely used in the past. However, the systemic absorption of aluminum from these agents and the potential toxicity associated with their use no longer make this type of binder a viable long-term treatment option.

Iron Deficiency Anemia

Anemia is a condition characterized by abnormally low levels of hemoglobin. Hemoglobin is contained within RBCs and carries oxygen to other parts of the body. If there are too few RBCs or if hemoglobin levels are low, the cells in the body will not get enough oxygen. IDA is a common form of anemia that is caused by patients not having enough iron to manufacture healthy RBCs. Although anyone can develop IDA, IDA is particularly common in patients with NDD-CKD. IDA is associated with fatigue, lethargy, decrease quality of life, cardiovascular complications, hospitalizations and increased mortality.

We estimate that there are more than 500,000 adult patients in the United States with NDD-CKD diagnosed with IDA. Currently, there are two forms of iron therapy used to treat IDA: oral iron supplements and iron delivered via intravenous infusion, or IV iron. Oral iron is currently the first-line iron replacement therapy for most physicians; however, oral iron supplements are poorly absorbed by many patients, which may adversely impact their effectiveness, and are associated with certain side effects, such as constipation, diarrhea and cramping, that may adversely affect patient compliance. IV iron is viewed as an effective treatment; however, like other intravenous medicines, it is logistically difficult to administer in an office setting, where NDD-CKD patients are more often treated.

Commercialization

We market Auryxia in the United States through our well-established, nephrology-focused sales force and commercial organization.

Auryxia, as an oral drug, is covered by Medicare only under Part D. We have gained access for Auryxia in the United States in both Medicare Part D and commercial channels. Auryxia is currently covered for the Hyperphosphatemia Indication in nine of the ten largest Medicare Part D plans, which provide coverage for approximately 35.8 million people, and the ten largest

commercial plans and pharmacy benefit managers in the United States, which provide coverage for approximately 131.0 million people. In September 2018, the Centers for Medicare & Medicaid Services, or CMS, decided that Auryxia would no longer be covered by Medicare for the IDA Indication. While this decision does not impact CMS coverage of the Hyperphosphatemia Indication, it requires all Auryxia prescriptions for Medicare patients to undergo a prior authorization to ensure their use in the Hyperphosphatemia Indication. On October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts against CMS and the U.S. Department of Health and Human Services challenging CMS's decision that Auryxia would no longer be covered by Medicare for the IDA Indication and imposing a prior authorization requirement for Auryxia in the Hyperphosphatemia Indication, or the CMS Decision. On October 22, 2021, the parties agreed to dismiss the litigation. See Part I, Item 3. Legal Proceedings for further information. While we believe that the vast majority of the Medicare prescriptions written for Auryxia today are for the Hyperphosphatemia Indication and therefore will continue to be covered by Medicare with prior authorization, the CMS Decision has had and will continue to have an adverse impact on the sales of Auryxia for the Hyperphosphatemia Indication and the IDA Indication.

JT, and its subsidiary, Torii, market Riona in Japan. We receive tiered double-digit royalties from JT and Torii based on their sales in Japan.

Manufacturing and Supply

Overview

We neither own nor operate, and currently have no plans to own or operate, any manufacturing or distribution facilities. We currently rely on third-party contract manufacturing organizations, or CMOs, to produce all of our preclinical and clinical material and commercial supply and third-party distributors to distribute Auryxia. We expect to continue to rely on either existing or alternative distributors and CMOs to distribute our products and supply our ongoing and planned preclinical studies and clinical trials and for commercial production. Our CMOs have other clients and may have other priorities that could affect their ability to perform the work satisfactorily and/or on a timely basis. Both of these occurrences would be beyond our control.

We have established relationships with several CMOs under which the CMOs manufacture preclinical, clinical and commercial supply of vadadustat drug substance and drug product, and clinical and commercial supply of Auryxia drug substance and drug product. All clinical and commercial supplies are manufactured under current Good Manufacturing Practices, or cGMPs, which is a regulatory standard for the production of pharmaceuticals that will be used in humans.

Vadadustat

We currently have redundant supply arrangements in place for the preclinical, clinical and commercial supply of vadadustat. We have entered into supply agreements with Esteve Química, S.A. and STA Pharmaceutical Hong Kong Limited, or STA, for the manufacture of vadadustat drug substance for commercial use and Patheon Inc. and STA for the manufacture of vadadustat drug product for commercial use. We plan to mitigate potential commercial supply risks for vadadustat, if any, through inventory management and additional redundant manufacturing arrangements for both drug substance and drug product and changes may occur following the launch of vadadustat, if approved.

Vadadustat is a small molecule. The synthesis of vadadustat is reliable and reproducible from starting materials available from multiple sources at commercially relevant scale using no unusual manufacturing equipment. Vadadustat can be formulated into compressed tablets using proprietary processes. As with any supply program, obtaining raw materials and finished drug product of the required quality and quantity cannot be guaranteed, and we cannot ensure that we will be successful in this endeavor.

Auryxia

We have established CMO relationships for the supply of Auryxia to help ensure that we will have sufficient material for ongoing commercial sales and clinical trials. The drug substance for Auryxia is supplied by Siegfried Evionnaz SA (two approved sites) and BioVectra Inc. (one approved site), pursuant to supply agreements with pricing structured on a per-kilogram basis. Consistent with our previously disclosed plans to lower the cost of goods sold for Auryxia, BioVectra and Keryx entered into an Amended and Restated Product Manufacture and Supply and Facility Construction Agreement on September 4, 2020. Auryxia drug product is supplied by Patheon Manufacturing Services LLC (Thermo Fisher) (three approved sites) pursuant to a Master Manufacturing Service Agreement with per-bottle pricing structured on a tiered basis, with the price reduced as the product volume increases. These agreements require that we satisfy certain minimum purchase requirements, but we are not obligated to use them as our sole suppliers. For more information about our manufacturing agreements for Auryxia, see Part II, Item 7. Management's Discussion and Analysis and Note 16 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data.

The active pharmaceutical ingredient of Auryxia, ferric citrate, is a small molecule. The synthesis of ferric citrate is reliable and reproducible from starting materials available from multiple sources at commercially relevant scale. Ferric citrate can be formulated into compressed tablets using proprietary manufacturing processes. As with any supply program, obtaining raw materials and finished drug product of the required quality and quantity cannot be guaranteed, and we cannot ensure that we will be successful in this endeavor.

We utilize third parties for the commercial distribution of Auryxia, including wholesale distributors and certain specialty pharmacy providers. We have also engaged Cardinal Health as the exclusive third-party logistics distribution agent for commercial sales of Auryxia.

License, Collaboration and Other Strategic Agreements

Vadadustat

U.S. Collaboration with Otsuka Pharmaceutical Co. Ltd.

On December 18, 2016, we entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement, pursuant to which we agreed to co-exclusively collaborate with Otsuka with respect to the development and commercialization of vadadustat in the United States, subject to the approval of vadadustat by the FDA. We are responsible for leading the development of vadadustat, for which we submitted an NDA to the FDA in March of 2021. We will co-commercialize vadadustat in the United States with Otsuka, subject to the approval of vadadustat by the FDA. We control and retain final decision-making authority with respect to certain matters, including U.S. pricing strategy and manufacturing.

Under the terms of the Otsuka U.S. Agreement, Otsuka paid us an upfront payment of $125.0 million and we expect Otsuka to provide additional funding of $393.9 million or more, depending on the actual costs incurred, toward the vadadustat global Phase 3 development program. This amount includes the Additional Funding (as defined below). Due to the costs incurred in completing the activities under the current global development plan exceeding a certain threshold in the second quarter of 2019, we elected to require Otsuka to increase the aggregate percentage of current global development costs it funds under the Otsuka U.S. Agreement and the Otsuka International Agreement, as defined below, from 52.5% to 80%, or the Otsuka Funding Option. The additional funding expected to result from having exercised the Otsuka Funding Option, or the Additional Funding, is fully creditable against future payments due to us under the arrangement, provided that future payments due to us may not be reduced by more than 50% in any calendar year and any remaining creditable amount above 50% in any calendar year will be applied to subsequent future payments until fully credited. We are eligible to receive from Otsuka up to $65.0 million in regulatory milestones and up to $575.0 million in specified commercial milestones.

The Otsuka U.S. Agreement establishes a profit share for the commercialization of vadadustat in the United States. The parties will equally share all net sales of vadadustat in the United States, if approved, and generally each party will bear half of all costs in the United States, including medical affairs, commercialization and manufacturing costs.

Under the Otsuka U.S. Agreement, we and Otsuka will jointly conduct all medical affairs and commercialization activities pursuant to plans agreed to by the parties. We will remain responsible for manufacturing vadadustat. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

Unless earlier terminated, the Otsuka U.S. Agreement will expire in the United States on a product-by-product basis on the date that one or more generic versions of vadadustat first achieves 90% market penetration. Either party may terminate the Otsuka U.S. Agreement in its entirety upon an uncured breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka U.S. Agreement in its entirety upon 12 months' prior written notice at any time after the release of the first top-line data from the global Phase 3 development program for vadadustat, which release occurred in the second quarter of 2020.

International Collaboration with Otsuka Pharmaceutical Co. Ltd.

On April 25, 2017, we entered into a collaboration and license agreement with Otsuka, or the Otsuka International Agreement, pursuant to which we granted Otsuka an exclusive license for the development and commercialization of vadadustat in certain territory outside the United States. The territory covered by the Otsuka International Agreement includes the European Union, Russia, China, Australia, Canada, the Middle East and certain other countries, or the Otsuka International Territory, but excludes Latin America and previously licensed jurisdictions. Under the Otsuka International Agreement, Otsuka is responsible for certain development activities and commercializing vadadustat in the Otsuka International Territory, while we led the global Phase 3 development program of vadadustat, and Otsuka submitted a MAA with the EMA in October 2021. Otsuka will fund a significant percentage of the costs of such global development program regardless of the total actual costs ultimately incurred. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

Under the terms of the Otsuka International Agreement, we expect Otsuka to pay us at least $317.7 million, comprised of $73.0 million that was paid upon execution of the Otsuka International Agreement and $244.8 million or more, depending on actual costs incurred, of development funding. In addition, we are eligible to receive from Otsuka up to $17.0 million in regulatory milestones for the licensed HIF product if we achieve the associated event within 12 to 24 months of the first HIF product approval and up to $525.0 million in commercial milestones. Otsuka also agreed to make tiered, escalating royalty payments ranging from low double digits up to thirty percent of net sales of vadadustat within the Otsuka International Territory. In limited circumstances, upper tier royalties may be subject to reduction if the supply price charged by us to Otsuka for vadadustat exceeds certain agreed upon thresholds, and royalty payments may also be reduced if a generic product is launched, on a country-by-country basis. Otsuka may elect to conduct additional studies of vadadustat in the European Union, subject to our right to delay such studies based on our objectives outside the Otsuka International Territory. Otsuka will pay a percentage of the costs of any such studies, and we will pay its portion of the costs in the form of a credit against future amounts due to us under the Otsuka International Agreement.

Unless earlier terminated, the Otsuka International Agreement will expire upon the expiration of the royalty term in the last country in the Otsuka International Territory. Either party may terminate the Otsuka International Agreement in its entirety upon an uncured material breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka International Agreement in its entirety or for a specific region in the Otsuka International Territory upon 12 months' prior written notice at any time after the release of the first top-line data from the global Phase 3 development program for vadadustat, which release occurred in the second quarter of 2020.

Collaboration with Mitsubishi Tanabe Pharma Corporation

On December 11, 2015, we entered into a collaboration agreement with MTPC, or the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries, or the MTPC Territory. In addition, we will supply vadadustat to MTPC for both clinical and commercial use in the MTPC Territory, subject to MTPC's option to manufacture commercial drug product in the MTPC Territory. On July 15, 2020, we entered into a supply agreement with MTPC for the commercial supply of vadadustat for use in Japan and certain other Asian countries, as contemplated by the MTPC Agreement.

We and MTPC agreed that, instead of including Japanese patients in our global Phase 3 program for vadadustat, MTPC would be the sponsor of a Phase 3 program for vadadustat in Japan. MTPC reported top-line data for the two Phase 3 pivotal trials and data from the two supportive Phase 3 studies in March 2019 and 52-week data for the two Phase 3 pivotal trials in November 2019. In June 2020, vadadustat was approved in Japan for the treatment of anemia due to CKD by the Ministry of Health, Labor and Welfare. In August 2020, MTPC launched vadadustat commercially in Japan under the trade name, Vafseo™, as a treatment of anemia due to CKD for adult patients on dialysis and not on dialysis. In January 2022, MTPC filed a new drug application for vadadustat for the treatment of anemia due to CKD in adult patients in Taiwan.

Unless earlier terminated, the MTPC Agreement will continue in effect on a country-by-country basis until the later of the following: expiration of the last-to-expire patent covering vadadustat in such country in the MTPC Territory; expiration of marketing or regulatory exclusivity in such country in the MTPC Territory; or ten years after the first commercial sale of vadadustat in such country in the MTPC Territory. MTPC may terminate the MTPC Agreement upon twelve months' notice at any time after the second anniversary of the effective date of the MTPC Agreement. Either party may terminate the MTPC Agreement upon the material breach of the other party that is not cured within a specified time period or upon the insolvency of the other party.

Under the terms of the MTPC Agreement, MTPC will make payments to us of up to approximately $225.0 million in the aggregate based on the achievement of certain development, regulatory and sales milestones, as well as tiered royalty payments ranging from 13% to 20% on annual net sales of vadadustat in the MTPC Territory, subject to reduction upon launch of a generic product on a country-by-country basis. MTPC was responsible for the costs of the Phase 3 program for vadadustat in Japan and other studies required in Japan and made no funding payments for our global Phase 3 program. Additionally, the development costs of approximately $20.5 million for our Phase 2 studies in Japan were reimbursed to us by MTPC. In February 2021, we entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or HCR, whereby we sold our right to receive royalties and sales milestones for vadadustat in Japan and certain other Asian countries in the MTPC territory under the MTPC Agreement. For more information on our royalty interest acquisition agreement with HCR, see Note 5 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

Vifor Pharma License Agreement

On February 18, 2022, we entered into the Vifor Second Amended Agreement with Vifor Pharma, which amended and restated the Vifor First Amended Agreement. Pursuant to the Vifor Second Amended Agreement, we granted Vifor Pharma an exclusive license to sell vadadustat to the Supply Group in the Territory. We currently retain rights to commercialize vadadustat for use in the non-dialysis dependent CKD market and to sell to dialysis organizations outside of the Supply Group. During the term of the Vifor Second Amended Agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the Territory to the Supply Group.

Like the Vifor First Amended Agreement, the Vifor Second Amended Agreement is structured as a profit share arrangement between us and Vifor Pharma in which we will receive approximately 66% of the profit, net of certain pre-specified costs. Under the Vifor First Amended Agreement, Vifor Pharma will make an upfront payment to us of $25 million in lieu of the previously disclosed milestone payment of $25 million that Vifor Pharma was to pay to us following approval of vadadustat by the FDA. In addition, Vifor Pharma made an equity investment in us, as further described below. We currently retain rights to commercialize vadadustat for use in the non-dialysis dependent CKD market and to sell to dialysis organizations outside of the Supply Group. As under the Vifor First Amended Agreement, during the term of the Vifor Second Amended Agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the Territory to the Supply Group.

As under the Vifor First Amended Agreement, the Vifor Second Amended Agreement provides that Akebia and Vifor Pharma will enter into a commercial supply agreement for vadadustat pursuant to which we will supply all of Vifor Pharma's requirements for vadadustat in the Territory. Under the Vifor Second Amended Agreement, Vifor Pharma will contribute $40 million to a working capital facility established to partially fund our costs of purchasing vadadustat from our contract manufacturers, which amount of funding will fluctuate, and which funding we will repay to Vifor Pharma over time.

Unless earlier terminated, the Vifor Second Amended Agreement will expire upon the later of the expiration of all patents that claim or cover vadadustat or the expiration of marketing or regulatory exclusivity for vadadustat in the Territory. Vifor Pharma may terminate the Vifor Second Amended Agreement in its entirety upon 30 months' prior written notice after the first anniversary of the receipt of regulatory approval, if approved, from the FDA for vadadustat for dialysis-dependent CKD patients. We may terminate the Vifor Second Amended Agreement in its entirety for convenience, following the earlier of a certain period of time elapsing or following certain specified regulatory events, and upon six months' prior written notice. If we so terminate for convenience, subject to a specified exception, we will pay a termination fee to Vifor Pharma. In addition, either party may, subject to a cure period, terminate the Vifor Second Amended Agreement in the event of the other party's uncured material breach or bankruptcy. We may also terminate the Vifor Second Amended Agreement upon the occurrence of certain other events. The Vifor Second Amended Agreement also continues to include a standstill provision and customary representations and warranties.

Also in connection with entering into the Vifor Second Amended Agreement, on February 18, 2022, we and Vifor Pharma entered into an Investment Agreement, or the Investment Agreement, pursuant to which we sold an aggregate of 4,000,000 shares of our common stock to Vifor Pharma for a total of $20.0 million dollars. For more information on the Vifor Second Amended Agreement and Investment Agreement with Vifor Pharma, see Note 18 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

Janssen Pharmaceutica NV Research and License Agreement

On February 9, 2017, we entered into a Research and License Agreement, the Janssen Agreement, with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, pursuant to which Janssen granted us an exclusive license under certain intellectual property rights to develop and commercialize worldwide certain HIF prolyl hydroxylase targeted compounds.

Under the terms of the Janssen Agreement, Janssen granted us a license for a three-year research term to conduct research on the HIF compound portfolio, which research term is now expired. During the research term, we could designate one or more compounds as candidates for development and commercialization. Once a compound was designated for development and commercialization, we were to be solely responsible for the development and commercialization of the compound worldwide at our own cost and expense.

Under the terms of the Janssen Agreement, we paid an upfront payment of $1.0 million in cash to Janssen and issued a warrant to purchase 509,611 shares of our common stock, which expired on February 9, 2022. In addition, Janssen could be eligible to receive up to an aggregate of $16.5 million from us in specified development milestone payments on a product-by-product basis. Janssen will also be eligible to receive up to $215.0 million from us in specified commercial milestones as well as tiered, escalating royalties ranging from a low to mid-single digit percentage of net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory.

Unless earlier terminated, the Janssen Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longer of the expiration of the patents licensed under the Janssen

Agreement, the expiration of regulatory exclusivity for such product, or 10 years from first commercial sale of such product. We may terminate the Janssen Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Janssen. The parties also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Janssen Agreement or in the event of certain additional circumstances.

As discussed above, we issued a Common Stock Purchase Warrant, or the Warrant, to Johnson & Johnson Innovation – JJDC, Inc., or JJDC, an affiliate of Janssen, for 509,611 shares of our common stock at an exercise price of $9.81 per share. The Warrant was issued without registration under the Securities Act of 1933, as amended, or the Securities Act. The Warrant was exercisable by JJDC, in whole or in part, at any time prior to February 9, 2022. We recorded the fair value of the Warrant in the amount of $3.4 million to additional paid-in capital and research and development expense in March 2017.

Cyclerion Therapeutics License Agreement

On June 4, 2021, we entered into the Cyclerion Agreement with Cyclerion, pursuant to which Cyclerion granted us an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral sGC stimulator.

Under the terms of the Cyclerion Agreement, we made an upfront payment of $3.0 million in cash to Cyclerion, which was paid during the second quarter of 2021. In addition, Cyclerion is eligible to receive up to an aggregate of $222.0 million from us in specified development and regulatory milestone payments on a product-by-product basis. Cyclerion will also be eligible to receive specified commercial milestones as well as tiered royalties ranging from a mid-single-digit to mid-teen percentage of net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory. We recorded the upfront payment in the amount of $3.0 million to research and development expense in June 2021.

Unless earlier terminated, the Cyclerion Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longest of (i) the expiration of the patents licensed under the Cyclerion Agreement, (ii) the expiration of regulatory exclusivity for such product, and (iii) 10 years from first commercial sale of such product. We may terminate the Cyclerion Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Cyclerion. We and Cyclerion also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Cyclerion Agreement or in the event of certain additional circumstances.

Auryxia

License Agreement with Panion & BF Biotech, Inc.

Prior to the Merger, Keryx entered into a license agreement, or the Panion License Agreement, which was amended from time to time, with Panion & BF Biotech, Inc., or Panion, under which Keryx in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, or the Licensor Territory, for the development and commercialization of ferric citrate.

On April 17, 2019, we and Panion entered into a second amended and restated license agreement, or the Panion Amended License Agreement, which amends and restates in full the Panion License Agreement. The Panion Amended License Agreement provides Keryx with an exclusive license under Panion-owned know-how and patents covering the rights to sublicense, develop, make, use, sell, offer for sale, import and export ferric citrate worldwide, excluding the Licensor Territory. The Panion Amended License Agreement also provides Panion with an exclusive license under Keryx-owned patents covering the rights to sublicense (with our written consent), develop, make, use, sell, offer for sale, import and export ferric citrate in certain countries in the Licensor Territory. Consistent with the Panion License Agreement, under the Panion Amended License Agreement, Panion is eligible to receive from us or any sublicensee royalty payments based on a mid-single digit percentage of sales of ferric citrate in our licensed territories. We are eligible to receive from Panion or any sublicensee royalty payments based on a mid-single digit percentage of net sales of ferric citrate in Panion's licensed territories.

The Panion Amended License Agreement terminates upon the expiration of each of our and Panion's obligations to pay royalties thereunder. In addition, we may terminate the Panion Amended License Agreement (i) in its entirety or (ii) with respect to one or more countries in our licensed territory, in either case upon 90 days' notice. We and Panion also each have the right to terminate the Panion Amended License Agreement upon the occurrence of a material breach of the Panion Amended License Agreement by the other party, subject to certain cure provisions, or certain insolvency events. The Panion Amended License Agreement also provides that, on a country-by-country basis, during the term and until the second anniversary of the expiration of our or Panion's obligation, as applicable, to pay royalties in a country in which such party has ferric citrate for sale on the date of such expiration, neither the other party nor its affiliates will, directly or indirectly, sell, distribute or otherwise commercialize or supply or cause to supply ferric citrate to a third party for sale or distribution in such country. In addition, the

Panion Amended License Agreement provides that each of us and Panion has the right, but not the obligation, to conduct litigation against any infringer of certain patent rights under the Panion Amended License Agreement in certain territories.

During the year-ended December 31, 2021, Panion earned $11.8 million in royalty payments relating to the sales of Auryxia in the United States and JT and Torii net sales of Riona in Japan, as we are required to pay a mid-single digit percent of JT and Torii's net sales of Riona in Japan to Panion under the terms of the Panion Amended License Agreement.

Sublicense Agreement with Japan Tobacco Inc. and Torii Pharmaceutical Co., Ltd.

In September 2007, Keryx entered into a Sublicense Agreement with JT and Torii, under which JT and Torii obtained the exclusive sublicense rights for the development and commercialization of ferric citrate in Japan. Effective June 8, 2009, Keryx entered into an Amended and Restated Sublicense Agreement, which was amended in June 2013, or the Revised Agreement, with JT and Torii.

In January 2014, JT and Torii received manufacturing and marketing approval of ferric citrate from the Japanese Ministry of Health, Labour and Welfare. Ferric citrate hydrate, which launched in May 2014 and is being marketed in Japan by Torii under the brand name Riona, is indicated as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including NDD-CKD and DD-CKD. In July 2019, JT and Torii, reported positive top-line results from a pivotal Phase 3 comparative study evaluating Riona for the treatment of IDA in adult patients in Japan, which was approved in March 2021. In May 2020, JT and Torii filed an application for approval of IDA as an additional indication for Riona in Japan. Under the terms of the Revised Agreement with JT and Torii, we are eligible to receive royalty payments based on a tiered low double-digit percentage of net sales of Riona in Japan inclusive of amounts that we must pay to Panion on JT and Torii's net sales of Riona under the Panion Amended License Agreement, subject to certain reductions upon expiration or termination of the Panion Amended License Agreement, and may also receive up to an additional $55.0 million upon the achievement of certain annual net sales milestones. We recorded $5.8 million in license revenue related to royalties earned on net sales of Riona in Japan during the twelve months ended December 31, 2021.

The sublicense under the Revised Agreement terminates upon the expiration of all underlying patent rights. Also, JT and Torii may terminate the Revised Agreement with or without cause upon at least six months prior written notice to us. Additionally, either party may terminate the Revised Agreement for cause upon 60 days' prior written notice after the breach of any uncured material provision of the Revised Agreement, or after certain insolvency events.

Intellectual Property

The proprietary nature of, and protection for, our products, product candidates and our discovery programs, processes and know-how are important to our business. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we may benefit from a variety of statutory frameworks in the United States, Europe and other countries that provide periods of non-patent-based exclusivity for qualifying molecules. See "—Regulatory Matters."

Our commercial success will depend in part on obtaining and maintaining patent protection of our current products as well as current and future product candidates, methods of their use and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our product candidates, discovery programs and processes. Even once patents successfully issue, third parties may challenge the validity, enforceability, inventorship, or scope thereof, which may result in such patents being narrowed, invalidated or held not infringed or unenforceable. For this and more comprehensive risks related to our intellectual property, please see "Risk Factors—Risks Related to Our Intellectual Property."

Individual patents extend for varying periods of time depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued from applications filed in the United States are effective for 20 years from the earliest filing date of a United States non-provisional application or an international application filed under the Patent Cooperation Treaty. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period,

however, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest international filing date. Patent term recapture for loss of term as a result of the regulatory review period is available in some foreign jurisdictions. In the United States, a patent's term may also be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office, or USPTO, in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

Changes in either the patent laws or interpretations of patent laws in the United States and other countries can diminish our ability to protect our inventions and enforce our intellectual property rights. Accordingly, we cannot predict the breadth or enforceability of claims that may be granted in our patents or in third-party patents. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to maintain and solidify our proprietary position for our drugs and technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of the patent applications that we may file or license from third parties will result in the issuance of any patents. The issued patents that we own or license or may receive or acquire in the future may be challenged, invalidated or circumvented, and the rights granted under any issued patents may not provide us with sufficient protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may be able to independently develop and commercialize similar drugs or duplicate our technology, business model or strategy without infringing our patents. Because of the extensive time required for clinical development and regulatory review of a drug we may develop, it is possible that, before any of our drugs can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent. The patent positions for vadadustat and Auryxia are summarized below.

Vadadustat Patent Portfolio

We hold 12 issued patents covering the composition of matter, polymorph, method of treating anemia, pharmaceutical compositions of vadadustat, and processes for manufacturing vadadustat in the United States and additional patents issued or pending in many other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil, Mexico, Russia, Israel and India. The expected expiration dates for these patents are between 2027 and 2034 plus any extensions or adjustments of term available under national law.

We also hold patents and patent applications directed to starting materials and intermediates in the processes for manufacturing vadadustat, dosing regimens, formulations, and various other aspects relating to the treatment of anemia using vadadustat that are expected to expire between 2032 and 2042 exclusive of possible patent term extensions or adjustments.

We have ongoing opposition and invalidity proceedings relating to vadadustat. See Part II, Item 3. Legal Proceedings for further information relating to these matters.

Auryxia Patent Portfolio

Pursuant to Keryx's license with Panion, we have the exclusive rights under a series of patents and patent applications to commercialize Auryxia worldwide, excluding certain Asian-Pacific countries. These patents and patent applications include claims directed to compositions of matter, pharmaceutical compositions, methods of treatment, as well as methods for the manufacture of Auryxia.

Keryx's patent rights include 15 issued U.S. patents listed in the Orange Book covering the composition of matter, method of treating hyperphosphatemia, and pharmaceutical compositions of Auryxia. The expected expiration dates for these patents are between 2022 and 2030 plus any additional patent term extensions that may be available.

Pursuant to the sublicense with our Japanese partner, Japan Tobacco Inc., or JT, and its subsidiary, Torii Pharmaceutical Co. Ltd., or Torii, we have exclusively sublicensed certain Japanese patent rights to JT and Torii. These sublicensed rights include several Japanese patents and pending patent applications with composition of matter claims and methods of use claims covering Riona, the trade name under which JT and Torii market ferric citrate in Japan. The expected expiration dates for these patents and pending patent applications are between 2022 and 2027. To date, to our knowledge, no contested proceedings or third-party claims have been lodged against any of these Japanese patents.

We received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet), filed certain complaints for patent infringement relating to such

ANDAs, and have entered into settlement and license agreements with each of the ANDA filers. See Part II, Item 3. Legal Proceedings for further information relating to these matters.

Other Intellectual Property Rights

We depend upon trademarks, trade secrets, know-how and continuing technological advances to develop and maintain our competitive position. To maintain the confidentiality of trade secrets and proprietary information, we require our employees, scientific advisors, consultants and collaborators, upon commencement of a relationship with us, to execute confidentiality agreements and, in the case of parties other than our research and development collaborators, to agree to assign their inventions to us. These agreements are designed to protect our proprietary information and to grant us ownership of technologies that are developed in connection with their relationship with us. These agreements may not, however, provide protection for our trade secrets in the event of unauthorized disclosure of such information.

In addition to patent protection, we may utilize orphan drug regulations, pediatric exclusivity or other provisions of the Food, Drug and Cosmetic Act of 1938, as amended, or FDCA, such as new chemical entity exclusivity or new formulation exclusivity, to provide market exclusivity for a drug candidate. In the United States, the FDA has the authority to grant additional data protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity may provide an additional six months which are added to the term of data protection as well as to the term of a relevant patent, to the extent these protections have not already expired. We may also seek to utilize market exclusivities in other territories. We cannot assure you that our drug products or any drug candidates we may acquire or in-license, will obtain such orphan drug designation, pediatric exclusivity, new chemical entity exclusivity or any other market exclusivity in the United States, European Union or any other territory, or that we will be the first to receive the respective regulatory approval for such drugs so as to be eligible for any market exclusivity protection.

Know-How

In addition to patents, we rely upon unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment provisions in the confidentiality agreements with our employees. These agreements are designed to protect our proprietary information and, in the case of the invention assignment provisions, to grant us ownership of technologies that are developed by our employees. These agreements may be breached, and we may not have adequate remedies for any breach.

To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

The Hatch-Waxman Act

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are usually not required to conduct, or submit results of, nonclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to make certain certifications to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a Section viii statement, certifying that its proposed ANDA label does not contain or carve out any language regarding the patented method-of-use, rather than certify to a listed method-of-use patent.

If the applicant does not challenge the listed patents, the ANDA will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months from receiving the Paragraph IV certification, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant. Also, the ANDA will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains an active moiety that has not been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which time the FDA cannot accept any ANDA seeking approval of a generic version of that drug. Certain changes to a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which the FDA cannot approve an ANDA for a generic drug that includes such changes.

An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

Patent Term Extension

After NDA approval, owners of relevant drug patents or their agents may apply for up to a five-year patent extension for delays caused by FDA regulatory review. The allowable patent term extension is calculated as half of the drug's testing phase which is the time between IND submission and NDA submission, and all of the review phase, which is the time between NDA submission and approval, up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years from the date of approval by virtue of the patent term extension.

We have filed applications under the patent term extension provisions of 35 U.S.C. § 156 for U.S. Patent Nos. 8,299,298, 8,093,423, 7,767,851, 5,753,706, and 8,338,642 each of which covers Auryxia for delays caused by FDA regulatory review. If granted, we can utilize the patent term extension on one of these patents, however, we cannot assure you that we can obtain any extension of the term of these patents. Upon expiration of these patents, competitors who obtain the requisite regulatory approval may potentially offer products with the same composition and/or method of use as our product, so long as the competitors do not infringe any other patents that we may own or license.

For patents that might expire before a determination regarding patent term extension, the patent owner or its agent may request an interim patent term extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the USPTO must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. We previously filed for and received interim patent term extension in accordance with 35 U.S.C. § 156(e)(2) for U.S. Patent No. 5,753,706 until February 3, 2022.

In addition, certain jurisdictions outside of the U.S., including Japan, have provisions that provide for patent term extension. In October 2014, following the regulatory approval of Riona in Japan, the Japan Patent office granted the patent term extensions filed by our sublicensee, JT, for Japanese Patents Nos. 4964585 and 4173553. As a result of the extension of patent term, Japanese Patents Nos. 4964585 and 4173553 will expire in November 2025 and November 2022, respectively.

In the future, if and when our product candidates, including vadadustat, receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each product candidate and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

Competition

The pharmaceutical and biotechnology industries are highly competitive. Our competitors include pharmaceutical companies and biotechnology companies, as well as universities and public and private research institutions. In addition, companies that are active in different but related fields represent substantial competition for us. Many of our competitors have significantly greater capital resources, larger research and development staffs and facilities and greater experience in drug development, regulation, manufacturing and marketing than we do. These organizations also compete with us to recruit qualified personnel, attract partners for joint ventures or other collaborations, and license technologies that are competitive with ours. To compete successfully in this industry, we must identify novel and unique drugs or methods of treatment and then complete the development of those drugs as treatments in advance of our competitors.

Vadadustat

Drugs that may compete with vadadustat, if approved, include Epogen® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa) and Eprex® (epoetin alfa), commercialized by Johnson & Johnson in the United States and Europe, respectively, and Mircera® (methoxy PEG-epoetin beta), commercialized by Vifor Pharma in the United States and Roche Holding Ltd. outside of the United States.

We and our partners may also face competition from potential new anemia therapies. There are several other HIF-PH inhibitor product candidates in various stages of development for anemia indications that may be in direct competition with vadadustat if and when they are approved and launched commercially. These candidates are being developed by companies such as FibroGen Inc., or FibroGen, together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, Japan Tobacco International, or JT, GlaxoSmithKline plc, or GSK, and Bayer HealthCare AG, or Bayer.

Furthermore, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable ESA utilization and thus limit the market potential for vadadustat if they are approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia that may impact the market for anemia-targeted treatment.

In addition, in the United States, FibroGen filed an NDA for its product candidate, roxadustat, with the FDA, but the FDA issued a complete response letter indicating the FDA will not approve the NDA in its present form. In Europe however, roxadustat is approved for the treatment of anemia in patients with CKD.

In Japan, Vafseo, which is approved for patients with CKD, including both DD-CKD and NDD-CKD, competes with roxadustat, daprodustat and enarodustat. Roxadustat is approved for the treatment of anemia due to CKD, including DD-CKD and NDD-CKD patients. In addition, daprodustat, GSK's product candidate, and enarodustat, JT's product candidate, are approved in Japan for the treatment of anemia due to CKD. In addition, Bayer HealthCare AG has submitted a new drug application for its product candidate for the treatment of renal anemia in Japan. In China, FibroGen launched roxadustat for the treatment of anemia of DD-CKD and for the treatment of anemia due to CKD in NDD-CKD patients.

A biosimilar is a biologic product that is approved based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product. The patents for the existing, branded biologic product must expire in a given market before biosimilars may enter that market without risk of being sued for patent infringement. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the existing, branded product was approved under a Biologics License Application, or BLA. The patents for epoetin alfa, an injectable ESA, expired in 2004 in the EU, and the remaining patents expired between 2012 and 2016 in the United States. Because injectable ESAs are biologic products, the introduction of biosimilars into the injectable ESA market in the United States will constitute additional competition for vadadustat if we are able to obtain approval for and commercially launch vadadustat. In the United States, Pfizer's biosimilar version of injectable ESAs, Retacrit® (epoetin alfa-epbx), was approved by the FDA in May 2018 and launched in November 2018 and several biosimilar versions of injectable ESAs are available for sale in the EU.

Furthermore, vadadustat's commercial opportunities, if approved, may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than vadadustat.

Auryxia

Hyperphosphatemia Competition

Auryxia is competing in the hyperphosphatemia market in the United States with other FDA-approved phosphate binders such as Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Sanofi, PhosLo® and Phoslyra® (calcium acetate), marketed by Fresenius Medical Care North America, Fosrenol® (lanthanum carbonate), marketed

by Shire Pharmaceuticals Group plc, and Velphoro® (sucroferric oxyhydroxide), marketed by Fresenius Medical Care North America, as well as over-the-counter calcium carbonate products such as TUMS® and metal-based options such as aluminum, lanthanum and magnesium. Most of the phosphate binders listed above are now also available in generic forms. In addition, other agents are in development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) or could otherwise enter the market, including Ardelyx, Inc.'s tenapanor (which is approved in the U.S. for the treatment of adults with irritable bowel syndrome with constipation, but for which the FDA issued a complete response letter with respect to the control of serum phosphorus in adult patients with CKD on dialysis), that may impact the market for Auryxia.

Iron Deficiency Anemia Competition

Auryxia is competing in the IDA market in the United States with over-the-counter oral iron, ferrous sulfate, other prescription oral iron formulations, including ferrous gluconate, ferrous fumerate, and polysaccharide iron complex, and intravenous iron formulations, including Feraheme® (ferumoxytol injection), Venofer® (iron sucrose injection), Ferrlicit® (sodium ferric gluconate complex in sucrose injection), Injectafer® (ferric carboxymaltose injection), and Triferic® (ferric pyrophosphate citrate). In addition, other new therapies for the treatment of IDA may impact the market for Auryxia, such as Shield Therapeutic' plc's Feraccru® (ferric maltol), which is available in Europe for the treatment of IDA, and Accrufer® (ferric maltol), which was launched in the United States for the treatment of IDA in July 2021.

Furthermore, Auryxia's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than Auryxia. Other companies have product candidates in various stages of preclinical or clinical development to treat diseases and complications of the diseases for which we are marketing Auryxia. In addition, we entered into settlement agreements with each of our ANDA filers pursuant to which we granted licenses to market a generic version of Auryxia in the United States beginning in March 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature, which may impact our business and results of operation.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, pricing, reimbursement, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory requirements, require the expenditure of substantial time and financial resources.

Review and Approval of Drug Products in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

Our product candidates must be approved by the FDA for therapeutic indications before we or our partners are able to market them in the United States. An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations and consistent with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, or ICH, requirements;
- design of a clinical protocol and submission to the FDA of an IND, which must be reviewed and active by the FDA before human clinical trials may begin;
- approval by an independent local or central institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed product candidate for each indication;
- preparation and submission to the FDA of an NDA requesting marketing for one or more proposed indications;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product candidate, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product candidate's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites and records to assure compliance with GCPs and good practices, or GxPs, the integrity of the clinical data and that adequate controls and oversight are in place regarding manufacturing, clinical trials, pharmacovigilance, safety, data management, vendor oversight, collection and reporting of serious adverse events and other activities;
- payment of user fees and securing FDA approval of an NDA; and
- compliance with any post-approval requirements and/or commitments, including the potential requirement to implement a risk evaluation and mitigation strategy, or REMS, and potentially post-market requirement, or PMR, and post-market commitment, or PMC, studies.

Preclinical Studies

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

Clinical trials involve the administration of the investigational product to human patients under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research patients provide their voluntary informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped through interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be obtained prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the submission of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research patients will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold or require that the sponsor amend the clinical protocol to include additional safety measurements. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin (or resume if the clinical trial had been ongoing at the time a clinical hold was imposed).

In addition to the foregoing requirements related to the IND submission, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to study patients. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if

the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived by the FDA. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee, or IEC, and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical trials. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data.

Reporting Clinical Trial Results

Under the Public Health Service Act, or PHSA, sponsors of clinical trials of certain FDA-regulated products, including prescription drugs and biologics, are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017, and both NIH and the FDA have recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors.

Specifically, the PHSA grants the Secretary of the U.S. Department of Health and Human Services, or HHS, the authority to issue a notice of noncompliance to a responsible party for failure to submit clinical trial information as required. The responsible party, however, is allowed 30 days to correct the noncompliance and submit the required information. The failure to submit clinical trial information to clinicaltrials.gov, as required, is also a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. In addition to civil monetary penalties, violations may also result in other regulatory action, such as injunction and/or criminal prosecution or disqualification from federal grants. Although the FDA has historically not enforced these reporting requirements due to HHS's long delay in issuing final implementing regulations, those regulations have now been issued and the FDA did issue its first Notice of Noncompliance to a manufacturer in April 2021.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

There is no obligation for a sponsor to make its investigational products available for expanded access; however, as required by amendments to the FDCA included in the 21st Century Cures Act, or the Cures Act, passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests with respect to product candidates in development to treat serious diseases or conditions, it must make that policy publicly available. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study for a covered investigational product; or 15 days after the investigational product receives designation from the FDA as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

On May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a

drug manufacturer to make its product candidates available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human patients under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research patients provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in four sequential phases, which may overlap or be combined:

- **Phase 1.** The product candidate is initially introduced into a small number of healthy human patients or, in certain indications such as cancer, patients with the target disease or condition (e.g., cancer) and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- **Phase 2.** The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- **Phase 3.** These clinical trials are commonly referred to as "pivotal" studies, which denote a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a product candidate. The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product candidate for approval, identify adverse effects, establish the overall risk-benefit profile of the product candidate and to provide adequate information for the labeling of the product candidate.
- **Phase 4.** Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Moreover, as noted above, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

Progress reports detailing the results of the clinical trials conducted under the IND must be submitted at least annually to the FDA and, more frequently, if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA, IRB or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

In response to the COVID-19 pandemic, the FDA issued guidance on March 18, 2020, and has updated it periodically since that time to address the conduct of clinical trials during the pandemic. The guidance sets out a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical study report (or as a separate document) contingency measures implemented to manage the study, and any disruption of the study as a result of COVID-19; a list of all study participants affected by COVID-19-related study disruptions by a unique subject identifier and by investigational site, and a description of how the individual's participation was altered; and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the study, among other things. The FDA has indicated that it will continue to provide any necessary guidance to sponsors, clinical investigators, and research institutions as the public health emergency evolves.

Pediatric Studies

Under the Pediatric Research Equity Act, or PREA, applications and certain types of supplements to applications must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor must submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-phase 2 meeting or as may be agreed between the sponsor and the FDA. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The sponsor and the FDA must reach agreement on a final plan. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical trials, early phase clinical trials, and/or other clinical development programs.

For investigational products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population.

Acceptance and Review of an NDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things are submitted to the FDA as part of an NDA requesting approval to market the product candidate for one or more indications. The fee required for the submission and review of an application under the Prescription Drug User Fee Act, or PDUFA, is substantial (for example, for fiscal year 2022 this application fee is approximately $3.1 million), and the sponsor of an approved application is also subject to an annual program fee, currently more than $369,000 per eligible prescription product. These fees are typically adjusted annually, and exemptions and waivers may be available under certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the applicant is a small business submitting its first human therapeutic application for review.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. This is known as the filing decision. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File determination to the applicant. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to certain performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. A product that has been designated as a breakthrough therapy may also be eligible for review within six months if supported by clinical data at the time of submission of the NDA. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component

manufacturing such as active pharmaceutical ingredients, finished drug product manufacturing, control testing laboratories, as well as packaging and labeling facilities. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. The applicant of the NDA may also have their records, processes, procedures, training, and other aspects reviewed during an inspection. The FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain drug applications, including applications for drugs in a shortage or drugs for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks.

Finally, the FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. The fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Improvement Act. This law established a new regulatory scheme allowing for expedited review of products designated as “breakthrough therapies.” A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's review clock goal for taking action on a marketing application from ten months to six months.

Priority Review Vouchers

A PRV is a voucher that the FDA issues to a sponsor of a rare pediatric disease or tropical disease product application at the time of the marketing application approval. Vouchers are transferable to other sponsors that may apply it to their NDAs or BLAs. A PRV entitles the holder to designate a single human drug application submitted under Section 505(b)(1) of the U.S. Federal Food, Drug, and Cosmetic Act or Section 351 of the Public Health Service Act as qualifying for a priority review. An FDA priority review may expedite the review process of a marketing application reducing the review time from ten months after formal acceptance of the file to six months after formal acceptance of the file. Applying the PRV to a marketing application does not ensure the FDA's approval of the marketing application and all requirements supporting the safety and efficacy of the product must be met. Our NDA submission for vadadustat did not include a PRV.

The FDA's Decision on an NDA

The FDA reviews an application to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term "substantial evidence" is defined under the FDCA as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. This approach was subsequently endorsed by Congress in 1998 with legislation providing, in pertinent part, that "If [FDA] determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, FDA may consider such data and evidence to constitute substantial evidence." This modification to the law recognized the potential for FDA to find that one adequate and well controlled clinical investigation with confirmatory evidence, including supportive data outside of a controlled trial, is sufficient to establish effectiveness. In December 2019, FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. It has not yet finalized that guidance.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter, or CRL, or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA or BLA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an "action package," which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision.
A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the applicant will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the applicant an additional six month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drugs and biologics within 30 days of approval of such products. To date, CRLs are not publicly available documents.

Post-Approval Requirements and Commitments

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, conditions of NDA approval may include sponsor agreement to PMR or PMC studies, which are designed to further assess drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. These may include additional studies, registries, data collection, analyses, and/or information.

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a product candidate's safety or effectiveness are prohibited before the product candidate is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA or in a manner that is inconsistent with the product's prescribing information. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

In the United States, healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific conditions, for a manufacturer to engage in nonpromotional, truthful and non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. In addition, companies may also promote information that it consistent with the prescribing information and have the ability to proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug under some relatively recent guidance from the FDA.

However, if a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the

manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws, the most recent of which is still in the process of being phased into the U.S. supply chain and regulatory framework. The Prescription Drug Marketing Act, or PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Today, both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Congress more recently enacted the Drug Supply Chain Security Act, or DSCSA, which made significant amendments to the FDCA, including by replacing certain provisions from the PDMA pertaining to wholesale distribution of prescription drugs with a more comprehensive statutory scheme. The DSCSA now requires uniform national standards for wholesale distribution and, for the first time, for third-party logistics providers; it also provides for preemption of certain state laws in the areas of licensure and prescription drug traceability.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical trials which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant. Products approved under Section 505(b)(2) are often referred to as follow-on products.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Under the Hatch-Waxman Act, the FDA may not approve an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a NCE. For the purposes of this provision, the FDA has consistently taken the position that an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, a generic or follow-on drug application may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs or 505(b)(2) applications seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

As part of the submission of an NDA or certain supplemental applications, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Upon approval of a new drug, each of the patents listed in the application for the drug is then published in the Orange Book. The FDA's regulations governing patent listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book. Specifically, the ANDA applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. Moreover, to the extent that the Section 505(b)(2) NDA applicant is relying on studies conducted for an already approved product, the applicant also is required to certify to the FDA concerning any patents listed for the NDA-approved product in the Orange Book to the same extent that an ANDA applicant would.

If the generic drug or follow-on drug applicant does not challenge the innovator's listed patents, FDA will not approve the ANDA or 505(b)(2) application until all the listed patents claiming the referenced product have expired. A certification that the new generic product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA owner and patent holders once the ANDA has been accepted for filing by the FDA. The NDA owner and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earliest of 30 months after the receipt of the Paragraph IV notice, expiration of the patent or a decision in the infringement case that is favorable to the ANDA or 505(b)(2) NDA application.

Pediatric Studies and Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing patent or regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product is effective in the pediatric population studied, rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, the HHS has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. While we are not a covered entity and thus HIPAA does not directly apply to us, we could be subject to penalties, including criminal penalties, if we knowingly obtain or further disclose PHI from a covered entity, such as a health care provider or clinical research site, and therefore we must ensure the proper authorizations are in place before we, or our vendors or business partners, obtain access to any PHI. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

At the state level, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers rights as it relates to their personal information, and allow for a new cause of action for data breaches. Additionally, effective starting on January 1, 2023, the California Privacy Rights Act, or CPRA, will significantly modify the CCPA, including by expanding consumers' rights, particularly with respect to certain sensitive personal information and creating new principles, such as data minimization, purpose limitation, and storage limitation. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The CCPA and CPRA could impact our business activities depending on how it is interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and individually identifiable health information. These provisions may apply to some of our business activities. In addition, other states already have passed state privacy laws. Other states will be considering these laws in the future. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products, if and once approved.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any

of which could adversely affect our ability to operate our business and our results of operations. To the extent that any product candidates we may develop, once approved, are sold in a foreign country, we may be subject to similar foreign laws.

Review and Approval of Drug Products Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Clinical Trial Approval in the European Union

Requirements for the conduct of clinical trials in the European Union including GCP are set forth in the Clinical Trials Directive 2001/20/EC, or the Clinical Trials Directive, and the GCP Directive 2005/28/EC, or the GCP Directive. Pursuant to the Clinical Trials Directive and the GCP Directive, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the EU member states. Under this system, approval must be obtained from the competent national authority of each EU member state in which a study is planned to be conducted. To this end, a clinical trial application, or CTA, is submitted to the local competent authority in each country, or Member State, where the clinical trial is being conducted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Clinical Trials Directive and the GCP Directive and other applicable guidance documents. These documents may be amended and/or updated by the European Commission at any time. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014, or the Clinical Trials Regulation, was adopted. The Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The new Clinical Trials Regulation is scheduled to come into application on January 31, 2022, following confirmation of full functionality of the Clinical Trials Information System through an independent audit by the European Commission in mid-2020. The Clinical Trials Regulation will come into application in all the EU Member States, repealing the current Clinical Trials Directive. The conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable at the end of January 2022. According to the transitional provisions, if a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable, the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the European Union at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the European Union

In March 2016, the EMA launched an initiative, the PRIority MEdicines, or PRIME, scheme, to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIME scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs,

may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated agency contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies are appointed early in the PRIME scheme, facilitating increased understanding of the product at the EMA's committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Pediatric Studies

Prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate because (a) the product is likely to be ineffective or unsafe in part or all of the pediatric population; (b) the disease or condition occurs only in adult population; or (c) the product does not represent a significant therapeutic benefit over existing treatments for pediatric population. Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

Marketing Authorization

To obtain marketing approval of a product under EU regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the CHMP established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various EU member states where such product has not received marketing approval in any EU member state before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

A marketing authorization may be granted only to an applicant established in the European Union. Once the marketing authorization is obtained in all member states of the European Union and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension. For orphan-designated medicinal products, the 10-year period of market exclusivity is extended to 12 years.

Conditional Approval

In particular circumstances, E.U. legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables applicants to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the product candidate is intended for the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases; (2) the product candidate is intended to meet unmet medical needs of patients; (3) a marketing authorization may be granted prior to submission of comprehensive clinical data provided that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required; (4) the risk-benefit balance of the product candidate is positive, and (5) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Periods of Authorization and Renewals in the European Union

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU member state. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the EU member state with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the EU member state decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU member state which delivered the marketing authorization within three years after authorization ceases to be valid.

Regulatory Data Exclusivity in the European Union

In the European Union, innovative medicinal products authorized in the European Union on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity. During this period, applicants for authorization of generics of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to a total of ten years' market exclusivity. During this ten-year period no generic of this medicinal product can be placed on the EU market. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a NCE so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Pediatric Exclusivity

If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent

protection through extension of the term of the Supplementary Protection Certificate, or SPC, or alternatively a one year extension of the regulatory market exclusivity from ten to eleven years, as selected by the marketing authorization holder.

Brexit and the Regulatory Framework in the United Kingdom

The U.K.'s withdrawal from the EU took place on January 31, 2020. The EU and the U.K. reached an agreement on their new partnership in the Trade and Cooperation Agreement, or the Agreement, which was applied provisionally beginning on January 1, 2021 and which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods, including healthcare products such as medicinal products. Thereafter, the EU and the U.K. will form two separate markets governed by two distinct regulatory and legal regimes. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the U.K. is no longer part of the single market. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law, the body of EU law instruments governing medicinal products that pre-existed prior to the U.K.'s withdrawal from the EU.

General Data Protection Regulation

Many countries outside of the United States maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or EEA, and the processing of personal data that takes place in the EEA, is subject to the European Union General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, providing notification of data breaches and taking certain measures when engaging third-party processors.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. This CJEU decision may lead to increased scrutiny on data transfers from the EU to the U.S. generally and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

As with other issues related to Brexit, there are open questions about how personal data will be protected in the U.K. and whether personal information can transfer from the EU to the U.K. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR. While the Data Protection Act 2018 in the U.K. that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the U.K., it is still unclear whether transfer of data from the EEA to the U.K. will remain lawful under GDPR. The U.K. government has already determined that it considers all European Union and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the U.K. to the European Union/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the U.K. as being "essentially adequate" for purposes of data transfer from the EU to the U.K., although this decision may be re-evaluated in the future.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and any eventual sale and distribution of commercial products.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication. In addition, third-party payors may impose prior authorization or step edit requirements requiring patients to have tried other therapies prior to our products for coverage. Payors may also decline to include our products or product candidates on their formulary, which means that unless healthcare providers seek a medical exception for coverage, the payors will not pay for the product.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

Dialysis-related drugs are included in the ESRD Bundle if they fall into functional categories such as anemia management and bone and mineral metabolism, except that oral-only drugs are exempted from inclusion until 2025. In a final ESRD PPS rule published in November 2018, CMS confirmed that it will expand the TDAPA to all new dialysis drugs approved by the FDA after January 1, 2020. The TDAPA provides separate payment for new drugs for two years based on the drug's Average Sales Price, or ASP, that will be in addition to the base rate in order to facilitate the adoption of innovative therapies. Although there are several details that need further clarification, including precise timing related to receiving codes to allow for reimbursement under TDAPA, which codes are assigned on a quarterly basis, the rule provides support for our assumption that new anemia treatments, including those in the HIF-PH inhibitor class, will be included in the ESRD Bundle and will be eligible for separate payment initially under TDAPA.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Dialysis Organizations Protocols

Dialysis organizations have their own formularies that list primary or preferred therapeutic options based on contracting status with drug manufacturers. While a prescriber may make their own independent decision to prescribe what they determine most appropriate for a given patient, any non-formulary therapeutic options are only available through an exception process based on clinical need. Similar to how payor coverage may affect the sales of a product, formulary status within dialysis organizations may affect what products are prescribed within that specific organization. Therefore, if a product is not on a formulary, the prescribers within that organization may be less likely to prescribe that product or may have a difficult time prescribing that product, resulting in less sales. Further, one dialysis organization's determination to add a product to their formulary does not assure that other dialysis organizations will also add the product to theirs. There is always a risk a dialysis organization will not contract with a drug manufacturer for a specific product, resulting in that product not being on that organization's formulary. Additionally, dialysis organizations typically assess a product's efficacy before adding it to their formulary. Their process for assessing a product may differ among organizations and the timing of such assessment could delay adding such treatment to formulary, further affecting product sales.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians, teaching hospitals and other healthcare providers, patient privacy laws and regulations, and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government
- HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which

impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the U.S. Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;
- the federal transparency requirements, known as the federal Physician Payments Sunshine Act (renamed the Open Payments Act), under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians, other healthcare providers and their immediate family members;
- the PDMA and its implementation regulations, as well as the DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by third-party payors, including private insurers, and state gift ban and disclosure law requirements that differ from the federal Physician Payments Sunshine Act in terms of the nature and type of transfers of value that are reportable and the types of covered recipients.

Violations of these laws are punishable by criminal and/or civil sanctions, including, in some instances, exclusion from participation in federal and state health care programs, such as Medicare and Medicaid. Ensuring compliance is time consuming and costly. Similar healthcare laws and regulations exist in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of personal information.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, such as the Pharmaceutical Research and Manufacturers of America Code on Interactions with Health Care Professionals, known as the PhRMA Code. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare.

In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has not been clearly defined. The ACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 203. Pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, and subsequent legislation, these Medicare sequester reductions have been suspended through the end of March 2022. From April 2022 through June 2022 a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the Tax Act, which was signed by the prior administration on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and, on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The prior administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new executive order that directs federal agencies to reconsider rules and other policies that limit access to healthcare, and consider actions that will protect and strengthen that access. Under this order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace

or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and under the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, the prior administration issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs the Department of Health and Human Services, or HHS, to create a plan within 45 days to combat “excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging.” On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Laws Relating to Foreign Trade

We are subject to various federal and foreign laws that govern our international business practices. These laws include the FCPA, which prohibits U.S. companies and their representatives from paying, offering to pay, promising, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate for the purposes of obtaining or retaining business, or to otherwise obtain favorable treatment or influence a person working in an official capacity. In many countries, the health care professionals we regularly interact with may meet the FCPA's definition of a foreign government official. Additionally, interactions with or on the part of our partners, collaborators, contract research organizations, vendors or other agents may also implicate the FCPA. The FCPA also requires public companies to make and keep books and records that accurately

and fairly reflect their transactions and to devise and maintain an adequate system of internal accounting controls. Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents unique challenges in the pharmaceutical industry because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments made by pharmaceutical companies to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Our international operations could also be subject to compliance with national laws of other countries, such as the United Kingdom Bribery Act. of 2010, or U.K. Bribery Act. The U.K. Bribery Act applies to any company "carrying on business" in the U.K., irrespective of where the offending conduct occurs. The U.K. Bribery Act applies to bribery activities both in the public and private sector and prohibits the provision of an "advantage" intended to induce or reward "improper performance" of the recipient's function. The failure by a company to prevent third parties from providing a bribe on its behalf could also constitute an offense. Penalties under the U.K. Bribery Act include potentially unlimited fines for companies and criminal sanctions for corporate officers under certain circumstances.

There are local antibribery and anticorruption laws in countries where we are conducting clinical trials, such as Brazil and Russia, and many of these also carry the risk of significant financial or criminal penalties. Our clinical trial operations could also result in enforcement actions by U.S., U.K., or other governmental authorities. There are also trade laws within the United States and in other regions that regulate the sale, purchase, import, export, reexport, transfer and shipment of goods, currency, products, materials, services and technology. Violations of these laws can lead to serious consequences, including substantial fines.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees and Human Capital Resources

As of December 31, 2021, we had 426 employees, all of whom were full-time. None of our employees are represented by any collective bargaining unit. We believe that we maintain good relations with our employees.

Retention, growth, training and development of our employees are integral to our success. We offer competitive compensation (including base salary, incentive bonus, and long-term equity awards tied to the value of our stock price) as well as benefits packages designed to attract, motivate and reward talented individuals who possess the skills necessary to support our business objectives, assist in the achievement of our strategic goals and create value for our stockholders. Our compensation program is designed to differentiate us from our talent competition and incentivize achievement of corporate goals, individual performance and demonstrate our corporate values. In addition, we provide development and leadership opportunities to our employees to cultivate talent throughout the Company.

We are committed to our employees' health, safety and well-being. In March 2020, in response to the COVID-19 pandemic, we adjusted our workplace policies to allow employees to work from home and in 2021 we remodeled our work paradigm to one that is flexible and designed to accommodate a range of work profiles from office based, to hybrid to fully remote, to field-based, allowing us to maximize productivity and performance. Further, in October 2021, to comply with federal, state and local mandates and guidelines, and in an effort to keep our employees safe, we announced a requirement that all of our employees be fully vaccinated by January 1, 2022, subject to medical and religious exemptions. Recognizing the pandemic has had an impact on well-being as well as the availability of support services, we recently launched Modern Health, a platform focused on services to support employees' and their dependents in areas such as mental, physical, financial, social and professional health, making it easier for them to get personalized care faster.

We are also committed to diversity, equality and inclusion, and this is reflected in Akebia's leadership. Two members of our Board of Directors, Cynthia Smith and LeAnne M. Zumwalt, are women, and women comprise approximately 45% of our senior management team. In addition, in November 2021, we appointed Ron Frieson to our Board of Directors.

With the goal of ensuring every employee is included, supported, and treated equitably, we developed a team (IDEA – Inclusion, Diversity & Equity Alliance) to support and guide Akebia as a diverse, inclusive, and culturally intelligent workplace. Over the past year this team has worked to identify areas for growth and education in order to develop processes, systems and actions that will enable us to continue to build an inclusive workplace and a diverse workforce. We also provide access to LinkedIn Learning, an online learning platform that recommends expert-led courses for relevant skill development for all of our employees.

In addition, we support kidney patient communities where we live and work. In the United States, we have a patient services program, Akebia Cares, designed to provide one-on-one support to help communicate individual benefits and available resources for patients today facing financial obstacles that keep them from accessing important medications. We also work closely with multiple kidney patient advocacy organizations, including the National Kidney Foundation, the American Kidney Fund, the Renal Support Network and Dialysis Patient Citizens. We believe our involvement with these organizations shows our commitment to our purpose of bettering the life of each person impacted by kidney disease.

Available Information

Our principal executive offices are located at 245 First Street, Cambridge, Massachusetts 02142. Our telephone number is (617) 871-2098. Our website address is www.akebia.com. The information on our website or that may be accessed by links on our website is not incorporated by reference into this Form 10-K. We make available, free of charge and through our website, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendments to any such reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after they are electronically filed with or furnished to the U.S. Securities and Exchange Commission.

Item 1A. Risk Factors

We face a variety of risks and uncertainties in our business. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also become important factors that affect our business. If any of the following risks occurs, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy

Our business is substantially dependent on the commercial success of Auryxia® (ferric citrate) and the regulatory approval and commercial success of vadadustat. If we do not obtain regulatory approval for vadadustat in the United States on a timely basis, or at all, or if we are unable to successfully commercialize current and future indications of Auryxia or vadadustat on a timely basis, or at all, our business, financial condition and future profitability will be materially harmed.

Our business and our ability to generate product revenue depend almost entirely on our, and our collaborators', ability to successfully commercialize Auryxia, obtain regulatory approval of vadadustat by the U.S. Food and Drug Administration, or FDA, and successfully commercialize vadadustat, if approved, and the level of market adoption for, and the continued use of, our products and product candidates, if approved. If we are not successful in obtaining regulatory approval for vadadustat, or commercializing any approved product, including achieving and maintaining an adequate level of market adoption, our profitability and our future business prospects will be adversely impacted.

Vadadustat is an investigational drug and is not approved by the FDA or any regulatory authority with the exception of Japan's Ministry of Health, Labour and Welfare. We submitted a New Drug Application, or NDA, to the FDA for vadadustat for the treatment of anemia due to chronic kidney disease, or CKD, in adult dialysis-dependent and non-dialysis dependent patients in March 2021 and the FDA assigned the application standard review and a Prescription Drug User Fee Act, or PDUFA, target action date of March 29, 2022. There is no guarantee that vadadustat will receive regulatory approval from the FDA by the PDUFA date, whether vadadustat will be approved at all and, if approved, whether the scope of approval will include the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. We will not be able to market or commercialize vadadustat in the United States unless and until it is approved. In the event that vadadustat does not receive regulatory approval on a timely basis, or at all, our financial condition would be materially harmed.

In addition, the success of Auryxia, vadadustat, if approved, and any current or future product candidates, including those that may be in-licensed or acquired, and our ability to generate product revenue and achieve profitability, depends on several factors, including:

- the timing and scope of marketing approvals for vadadustat and any other product candidate, if approved, including those that may be in-licensed or acquired;
- maintaining marketing approvals for Auryxia, vadadustat, if approved, and any other product, including those that may be in-licensed or acquired;
- obtaining adequate or favorable pricing and reimbursement from private and governmental payors for Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- obtaining and maintaining market acceptance of Auryxia, vadadustat, if approved, and any other product candidate, including those that may be in-licensed or acquired;
- the size of any market in which Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, receives approval and obtaining adequate market share in those markets;
- actual or perceived advantages or disadvantages of our products or product candidates as compared to alternative treatments, including their respective safety, tolerability and efficacy profiles, the potential convenience and ease of administration and cost;
- maintaining an acceptable safety and tolerability profile of our approved products, including the frequency and severity of any side effects;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, based, in part, on their perception of our clinical trial data and/or the actual or perceived safety, tolerability and efficacy profile;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate supplies of products that are compliant with good manufacturing practices, or GMPs, to support the clinical development and the market demand for Auryxia, vadadustat, if approved, and any other product and product candidate, including those that may be in-licensed or acquired;
- current and future restrictions or limitations on our approved or future indications and patient populations or other adverse regulatory actions or in the event that the FDA requires Risk Evaluation and Mitigation Strategies, or REMS, or risk management plans that use restrictive risk minimization strategies;
- the effectiveness of our sales, marketing, manufacturing and distribution strategies and operations;

- competing effectively with any products for the same or similar indications as our products;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents and trade secrets; and
- the impact of the novel coronavirus disease, or COVID-19, pandemic on the above factors, including the limitation of our sales professionals to meet in person with healthcare professionals as the result of travel restrictions or limitations on access for non-patients.

Market acceptance is critical to our ability to generate significant product revenue. Any product may achieve only limited market acceptance or none at all. If any of our approved products is not accepted by the market to the extent that we expect or market acceptance decreases, we may not be able to generate significant product revenue and our business would be materially harmed. Market acceptance of any approved product depends on a number of other factors, including:

- the availability of adequate coverage and reimbursement by and the availability of discounts, rebates and price concessions from third party payors, pharmacy benefit managers, or PBMs, and governmental authorities;
- the safety and efficacy of the product, as demonstrated in clinical trials and in the post-marketing setting;
- the prevalence and complications of the disease treated by the product;
- the clinical indications for which the product is approved and the product label approved by regulatory authorities, including any warnings or limitations that may be required on the label as a consequence of potential safety risks associated with the product;
- the countries in which marketing approvals are obtained;
- the claims we and our collaborators are able to make regarding the safety and efficacy of the product;
- the success of our physician and patient communications and education programs;
- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;
- the cost, safety and efficacy of the product in relation to alternative treatments;
- the timing of receipt of marketing approvals and product launch relative to competing products and potential generic entrants;
- relative convenience and ease of administration;
- the frequency and severity of adverse side effects;
- favorable or adverse publicity about our products or favorable or adverse publicity about competing products;
- the effectiveness of our and our collaborators' sales, marketing and distribution efforts; and
- the restrictions on the use of the product together with other medications, if any.

We have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses and cannot guarantee when, if ever, we will become profitable or attain positive cash flows.

Investment in pharmaceutical product development and commercialization is highly speculative because it requires upfront capital expenditures and there is significant risk that a product candidate will fail to gain marketing approval or that an approved product will not be commercially viable. Since our inception, we have devoted most of our resources to research and development, including our preclinical and clinical development activities and, following the merger, or the Merger, whereby Keryx Biopharmaceuticals, Inc., or Keryx, became a wholly owned subsidiary of ours, commercialization. We have financed our operations primarily through sales of equity securities, our strategic collaborations and, following the Merger, product revenues, a royalty monetization transaction and debt. Prior to the Merger, we had no products approved for commercial sale and had not generated any revenue from the sale of products. We are not currently profitable and have incurred net losses each year since our inception, including net losses of $282.8 million for the year ended December 31, 2021. As of December 31, 2021, we had an accumulated deficit of $1.5 billion. We cannot guarantee when, if ever, we will become profitable.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on product revenue, collaboration revenue, and our ability to obtain additional funding. We expect to continue to incur significant expenses if and as we:

- conduct and enroll patients in any clinical trials, including post-marketing studies or any other clinical trials for Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- continue our commercialization activities for Auryxia and vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired;
- maintain marketing approvals for Auryxia, vadadustat, if approved, and any other product, including those that may be in-licensed or acquired;
- have Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, manufactured for clinical trials and for commercial sale;

- conduct discovery and development activities for additional product candidates or platforms that may lead to the discovery of additional product candidates;
- engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would market and develop commercial products, or develop and commercialize other product candidates and technologies;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract, hire and retain qualified personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- experience any delays or encounter issues with any of the above.

We have and will continue to expend significant resources in our legal proceedings, as described under Part I, Item 3. Legal Proceedings, or any other legal proceedings brought by or against us in the future.

Because of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of increased expenses. The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter, the progress of our clinical development and our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

Even if we succeed in receiving marketing approval for, and are able to commercialize vadadustat in the United States and other regions, we will continue to incur substantial expenditures relating to continued commercialization and post-marketing requirements for Auryxia, vadadustat and any other products, including those that may be in-licensed or acquired, as well as costs relating to the research and development of any other product candidate, including those that may be in-licensed or acquired. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency, or the EMA, or other regulatory authorities, or if we otherwise believe it is necessary, to change our manufacturing processes or assays, to amend or replace our study protocols, to conduct any additional clinical trials, whether in order to obtain approval or as a post-approval study, to perform studies in addition to, different from or larger than those currently planned, if there are any delays in completing our clinical trials or if there are delays in or issues with obtaining marketing approval for vadadustat in the United States, the European Union, or EU, or other jurisdictions. In addition, our ability to generate revenue would be negatively affected if the size of our addressable patient population is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we sought or the patient population for treatment is narrowed by competition, physician choice, coverage or reimbursement, or payor or treatment guidelines. Even though we generate product revenue from Auryxia and royalties from Riona and Vafseo™, in Japan and may generate revenue and royalties from the sale of any products that may be approved in the future, including those that may be in-licensed or acquired, we may never generate revenue and royalties that are significant enough for us to become and remain profitable, and we will need to obtain additional funding to continue operations.

We will require substantial additional financing to achieve our goals. A failure to obtain this necessary capital when needed, or on acceptable terms, could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

As of December 31, 2021, our cash and cash equivalents and available for sale securities were $149.8 million. We expect to continue to expend substantial amounts of cash for the foreseeable future as we continue to commercialize Auryxia and seek regulatory approval for and commercialize vadadustat, if approved, and develop and commercialize any other product or product candidate, including those that may be in-licensed or acquired. These expenditures will include costs associated with research and development, manufacturing, potentially obtaining marketing approvals and marketing products approved for sale. In addition, other unanticipated costs may arise. Because the outcome of our current and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amount of funding necessary to successfully complete clinical development for any current or future product candidates, including vadadustat if additional clinical trials are required in order to obtain marketing approval, or to complete post-marketing studies for Auryxia and vadadustat, if approved. Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of conducting clinical trials or any post-marketing requirements or any other clinical trials for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired;
- the cost and timing of commercialization activities, including product manufacturing, marketing, sales and distribution costs, for Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- the results of our meetings with the FDA, the EMA and other regulatory authorities and any consequential effects, including on timing of and ability to obtain and maintain marketing approval, study design, study size and resulting operating costs;
- difficulties or delays in enrolling patients in our clinical trials;
- the outcome of our efforts to obtain marketing approval for vadadustat in the United States, Europe and in other jurisdictions and any other product candidates, including those that may be in-licensed or acquired, including any additional clinical trials or post-approval commitments imposed by regulatory authorities;
- the timing of, and the costs involved in obtaining, marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired, including to fund the preparation, filing and prosecution of regulatory submissions;
- the costs of maintaining marketing approvals for Auryxia or any other product, including those that may be in-licensed or acquired;
- the cost of securing and validating commercial manufacturing for any of our product candidates, including those that may be in-licensed or acquired, and maintaining our manufacturing arrangements for Auryxia and vadadustat or any other product, including those that may be in-licensed or acquired, or securing and validating additional arrangements;
- the costs involved in preparing, filing and prosecuting patent applications and maintaining, defending and enforcing our intellectual property rights, including litigation costs, and the outcome of such litigation;
- the costs involved in any legal proceedings to which we are a party;
- our ability to attract, hire and retain qualified personnel;
- any ongoing costs related to the creation of additional infrastructure and expansion of additional resources to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- the extent to which we engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would develop and market commercial products, or develop other product candidates and technologies.

Furthermore, we expect to continue to incur costs associated with operating as a fully integrated, publicly traded biopharmaceutical company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We expect our cash resources to fund our current operating plan through at least the next twelve months from the filing of this Annual Report on Form 10-K. We have based these estimates on assumptions that may prove to be wrong due to a variety of factors, including due to the effects of the ongoing COVID-19 pandemic, and we could use our available capital resources sooner than we currently expect. However, the potential timely regulatory approval of vadadustat and the receipt of associated regulatory milestones is an important source of funding of our cash runway, which are outside of our control. We expect to finance future cash needs through product revenue, public or private equity or debt transactions, payments from our collaborators (including associated regulatory approval milestones), royalty transactions, strategic transactions, or a combination of these approaches. In any event, we will require additional funding to fund our operating plan beyond the next twelve months, including to pursue development and commercial activities related to Auryxia and vadadustat, if approved, or any additional products and product candidates, including those that may be in-licensed or acquired. If we are unable to obtain sufficient funding, we could be required to delay our development efforts, limit activities and reduce costs, which could adversely affect our business prospects. There can be no assurance, that the current operating plan will be achieved in the time frame anticipated by us, or that its cash resources will fund our operating plan for the period anticipated by us or that additional funding will be available on terms acceptable to us, or at all.

Any additional fundraising efforts may divert our management’s attention away from their day-to-day activities, which may adversely affect our ability to develop and commercialize Auryxia, vadadustat and any other products or product candidates, including those that may be in-licensed or acquired. Also, additional funds may not be available to us in sufficient amounts or on acceptable terms or at all. If we are unable to raise additional capital in sufficient amounts when needed or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development and/or commercialization of Auryxia, vadadustat, if approved, and any other products or product candidates, including those that may be in-licensed or acquired. Any of these events could significantly harm our business, financial condition and prospects.

Our independent registered public accounting firm has included an explanatory paragraph relating to our ability to continue as a going concern in its report on our audited financial statements included in this Annual Report on Form 10-K.

We believe that our cash resources will be sufficient to fund our current operating plan through at least the next twelve months from the filing of our 2021 Annual Report on Form 10-K. However, there are conditions or events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern within twelve months after the date the financial statements are issued and certain elements of our operating plan are outside of our control, including the potential regulatory approval of vadadustat and the receipt of associated regulatory milestones, that cannot be considered probable. Therefore, the report from our independent registered public accounting firm for the year ended December 31, 2021 includes an explanatory paragraph stating that our losses from operations and required additional funding to finance our operations raise substantial doubt about our ability to continue as a going concern for a period of one year after the date the financial statements are issued. See Note 1 to our consolidated financial statements appearing elsewhere in our Annual Report on Form 10-K for additional information on our assessment.

If we are unable to obtain sufficient funding, our business, prospects, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms or at all. There can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, or that our cash resources will fund our operating plan for the period anticipated by the Company or that additional funding will be available on terms acceptable to us, or at all.

Pursuant to covenants in the Loan Agreement, as amended by the First Amendment and Waiver, our Quarterly Reports on Form 10-Q for the fiscal quarters ending June 30, 2022 and September 30, 2022 and our Annual Report on Form 10-K thereafter, must not be subject to any qualification as to going concern. If we do not satisfy the covenant as to going concern in any of these filings, we will be in default under the Loan Agreement. If an event of default occurs and is continuing under the Loan Agreement, the Collateral Agent is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement, which we may not have the available cash resources to repay at such time. If we are required to repay amounts due under the Loan Agreement earlier than anticipated, it could have a material adverse effect on our business, results of operations and financial condition.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product and product candidates on unfavorable terms to us.

We expect to finance our cash needs through product revenues, public or private equity or debt transactions, payments from our collaborators, royalty transactions, strategic transactions, or a combination of these approaches. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, our fixed payment obligations may increase, any such securities may have rights senior to those of our common stock, and the terms may include liquidation or other preferences and anti-dilution protections that adversely affect the rights of our common stockholders. Additional debt financing, if available, may involve agreements that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, make capital expenditures, declare dividends, acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through royalty transactions, we may have to relinquish valuable rights to our portfolio and future revenue streams, and enter into agreements that would restrict our operations and strategic flexibility. If we raise additional funds through strategic transactions with third parties, we may have to do so at an earlier stage than otherwise would be desirable. In connection with any such strategic transactions, we may be required to relinquish valuable rights to our product and product candidates, future revenue streams or research programs or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds when needed, we may not be able to pursue planned development and commercialization activities and we may need to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We may not be successful in our efforts to identify, acquire, in-license, discover, develop and commercialize additional products or product candidates or our decisions to prioritize the development of certain product candidates over others may not be successful, which could impair our ability to grow.

Although we continue to focus a substantial amount of our efforts on the commercialization of Auryxia and seeking regulatory approval for, and potential commercialization of, vadadustat, a key element of our long-term growth strategy is to develop additional product candidates and acquire, in-license, develop and/or market additional products and product candidates.

Research programs to identify product candidates require substantial technical, financial and human resources, regardless of whether product candidates are ultimately identified. Our research and development programs may initially show promise, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;
- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;
- a product candidate may be shown to have harmful side effects, a lack of efficacy or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and/or achieve market acceptance ;
- product candidates we develop may nevertheless be covered by third party patents or other exclusive rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer commercially reasonable;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- a product candidate may not be accepted as safe and effective by patients, the medical community, or third party payors, if applicable.

If any of these events occur, we may be forced to abandon our research and development efforts for one or more of our programs, or we may not be able to identify, discover, develop or commercialize additional product candidates, which may have a material adverse effect on our business.

Because we have limited financial and managerial resources, we focus on products, research programs and product candidates for specific indications. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications, or outlicense rights to product candidates, that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

Because our internal research capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists, and other researchers to sell or license product candidates, products or technology to us. The success of this strategy depends partly upon our ability to identify, select, and acquire promising product candidates and products. The process of identifying, selecting, negotiating and implementing a license or acquisition of a product candidate or an approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of a product candidate or an approved product. We have limited resources to identify and execute the acquisition or in-licensing of third party products, businesses, and technologies and integrate them into our current infrastructure.

Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. Any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA, the EMA, the Japanese Pharmaceuticals and Medical Devices Agency, or PMDA, or other regulatory authorities, or post-approval testing or other requirements if approved. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any of our products will be manufactured profitably, achieve market acceptance or not require substantial post-marketing clinical trials.

Accordingly, there can be no assurance that we will ever be able to identify, acquire, in-license or develop suitable additional products or product candidates, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential products, product candidates or other programs that ultimately prove to be unsuccessful.

We may engage in strategic transactions to acquire assets, businesses, or rights to products, product candidates or technologies or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt, or cause us to incur significant expense.

As part of our business strategy, we may engage in additional strategic transactions to expand and diversify our portfolio, including through the acquisition or in-license of assets, businesses, or rights to products, product candidates or technologies or through strategic alliances or collaborations, similar to the Merger and our existing collaboration and license arrangements. We may not identify suitable strategic transactions, or complete such transactions in a timely manner, on favorable terms, on a cost-effective basis, or at all. Moreover, we may devote resources to potential opportunities that are never completed or we may incorrectly judge the value or worth of such opportunities. Even if we successfully execute a strategic transaction, we may not be able to realize the anticipated benefits of such transaction and may experience losses related to our investments in such transactions. Integration of an acquired company or assets into our existing business may not be successful and may disrupt

ongoing operations, require the hiring of additional personnel and the implementation and integration of additional internal systems and infrastructure, and require management resources that would otherwise focus on developing our existing business. Even if we are able to achieve the long-term benefits of a strategic transaction, our expenses and short-term costs may increase materially and adversely affect our liquidity. Any of the foregoing could have a detrimental effect on our business, results of operations and financial condition. For example, on June 4, 2021, we entered into a License Agreement, the Cyclerion Agreement, with Cyclerion Therapeutics Inc., or Cyclerion, pursuant to which Cyclerion granted us an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase, or sGC, stimulator. If we are unsuccessful in developing praliciguat or if any of the assumptions that we made in valuing the transaction, including the costs of development, were incorrect, we may not recognize the anticipated benefits of the transaction and our business could be harmed.

In addition, future transactions may entail numerous operational, financial and legal risks, including:

- incurring substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- exposure to known and unknown liabilities, including contingent liabilities, possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- higher than expected acquisition and integration costs;
- difficulty in integrating operations, processes, systems and personnel of any acquired business;
- increased amortization expenses or, in the case of a write-down of the value of acquired assets, impairment losses, such as the Auryxia intangible asset impairment in the second quarter of 2020 and corresponding adjustments to the estimated useful life of the developed product rights for Auryxia;
- impairment of relationships with key suppliers or customers of any acquired business due to changes in management and ownership;
- inability to retain personnel, customers, distributors, vendors and other business partners integral to an in-licensed or acquired product, product candidate or technology;
- potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges;
- entry into indications or markets in which we have no or limited development or commercial experience and where competitors in such markets have stronger market positions; and
- other challenges associated with managing an increasingly diversified business.

If we are unable to successfully manage any transaction in which we may engage, our ability to develop new products and continue to expand and diversify our portfolio may be limited.

Our business has been and may continue to be, directly or indirectly, adversely affected by the COVID-19 pandemic.

The ongoing COVID-19 pandemic has presented a substantial public health and economic challenge around the world and continues to affect our employees, patients, healthcare providers with whom we interact, customers, collaboration partners, contract research organizations, or CROs, our contract manufacturing organizations, or CMOs, vendors, communities and business operations. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition continues to depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, any resurgences or variants of COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets where the healthcare providers with whom we interact, our partners, our CROs, our CMOs, and our other vendors operate.

We believe our revenue growth was negatively impacted by the COVID-19 pandemic in 2021 primarily as the CKD patient populations that we serve continue to experience both high hospitalization and mortality rates due to COVID-19. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, COVID-19 continues to adversely and disproportionately impact CKD patients; therefore, we expect COVID-19 to continue to have a negative impact on our revenue growth for the foreseeable future.

The majority of our office-based employees began working from home in March 2020 and continue to primarily work from home. While most of our office-based operations can be performed remotely, there is no guarantee that we will continue to be as effective while working remotely because our team is dispersed, which has limited valuable in person employee team interactions, and employees may become sick themselves and be unable to work. Further, our increased reliance on remote access to our information systems increases our exposure to potential cybersecurity breaches.

Moreover, our future success and profitability substantially depends on the management skills of our executives and certain other key employees. The unanticipated loss or unavailability of key employees due to the pandemic could harm our ability to operate our business or execute our business strategy and we may not be successful in finding and integrating suitable successors in the event of key employee loss or unavailability. For example, as of January 1, 2022, we have required all of our employees be fully vaccinated, subject to limited medical and religions exemptions in accordance with applicable laws. At this time, it is not possible to predict with certainty the exact impact that our vaccine requirement will continue to have on us or on our workforce. The vaccine requirement has resulted, and may continue to result, in employee distraction and could result in litigation and difficulty securing future labor need. This could have an adverse effect on our business, results of operations and cash flows.

In addition, several healthcare facilities have previously restricted access for non-patients, including the members of our sales force. For example, DaVita, Inc., or DaVita, and Fresenius Medical Care, or Fresenius, which account for a vast majority of the dialysis population in the United States, have previously restricted access to their clinics. As a result, we continue to engage with some healthcare providers and other customers virtually, where possible. The restrictions on our customer-facing employees' in-person interactions with healthcare providers has, and could continue to, negatively impact our access to healthcare providers and, ultimately, our sales, including with respect to vadadustat, if approved. Recently, such precautionary measures have been relaxed at certain healthcare facilities and, as a result, members of our sales force have resumed in person interactions with certain customers. Nevertheless, some restrictions remain, and more restrictions may be put in place again due to a resurgence in COVID-19 cases, including those involving new variants of COVID-19, which may be more contagious and more severe than prior strains of the virus. Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand for Auryxia and will be for vadadustat, if approved including the potential for further declines or changes in prescription trends and customer orders, which could have a material adverse effect on our business, results of operations, and financial condition.

In addition, the direct and indirect impacts of the pandemic or the response efforts to the pandemic, including, among others, competition for labor and resources and increases in labor, sourcing, manufacturing and shipping costs, may cause disruptions to, closures of or other impacts on our CMOs and other vendors in our supply chain on which we rely for the supply of our products and product candidates. At this time, our CMOs continue to operate at or near normal levels. However, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our contract manufacturers' ability to manufacture and deliver Auryxia and vadadustat (if approved in the United States and which is currently marketed under the trade name Vafseo™ by MTPC in Japan), which may result in increased costs and delays, or disruptions to the manufacturing and supply of our products. These impacts could have a negative effect on our inventory reserves, which could result in an increase in inventory write-offs due to expiry.

The pandemic has resulted in closures of and may continue to impact clinical trial sites on which we rely and will rely on in the future for the completion of certain clinical trials. COVID-19 pandemic precautions have caused moderate delays in enrolling new clinical trials and may cause delays in enrolling future clinical trials. Further, the pandemic has impacted and is likely to continue to impact the business of the FDA, the EMA and other government authorities, which potentially could result in delays in meetings, reviews, inspections and approvals relating to our product and product candidates. Any decision by the FDA, EMA or other governmental authorities to delay meeting with us or our collaboration partners or delay scheduling inspections in light of COVID-19 could have a material adverse effect on clinical trials of our product candidates or on our efforts to obtain marketing approvals for vadadustat, which could increase our operating expenses and have a material adverse effect on our financial results, including the timing and amount of future regulatory milestones we could receive from our collaboration partners.

If we or any of the third parties with whom we engage, including our collaboration partners, were to experience further shutdowns, delays or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted, which could have a material adverse effect on our business and our financial results.

The COVID-19 pandemic may continue to significantly impact economies and financial markets worldwide, which could result in adverse effects on our business and operations, impact our ability to raise additional funds and impact the volatility of our stock price and trading in our stock. Even after the COVID-19 pandemic has been contained or mitigated, we may continue to experience adverse impacts to our business as a result of any economic recession or depression that has occurred or may occur in the future.

The global impact of COVID-19 continues to rapidly evolve, and we will continue to monitor the situation closely. In particular, areas we are monitoring include possible COVID-related changes in our commercial revenue payor mix, overall product sales, and reserves and allowances, as well as negative trends that could potentially have a further significant impact on product demand and, ultimately, product revenue, or could cause goodwill, intangible assets, and other assets to be impaired. This uncertain pandemic environment has presented new risks to our business. While we are working to mitigate the impacts on

our business, we are mindful that many of these risks and the impact to the larger healthcare market are outside of our control. The extent to which COVID-19 impacts our business will depend on future developments, which are highly uncertain and the magnitude of which cannot be predicted, including new information that may emerge concerning the severity of COVID-19 and the actions to contain COVID-19, and the effectiveness of vaccines against virus variants.

Risks Related to our Financial Arrangements

Our obligations in connection with the loan agreement with Pharmakon and requirements and restrictions in the loan agreement could adversely affect our financial condition and restrict our operations.

In November 2019, we entered into a loan agreement with funds managed by Pharmakon Advisors LP, or Pharmakon, pursuant to which senior secured term loans in an aggregate principal amount of $100.0 million, or the Term Loans, were made available to us in two tranches. The first tranche of $80.0 million closed on November 25, 2019, and the second tranche of $20.0 million closed on December 10, 2020. We entered into a First Amendment and Waiver to the Loan Agreement with Pharmakon in February 2022. See Note 11 to our audited condensed consolidated financial statements in Part II, Item 8. Financial Statements of this Annual Report on Form 10-K for additional information regarding our obligations under the loan agreement, as amended, or the Loan Agreement.

The Loan Agreement contains affirmative and negative covenants applicable to us and our subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold, which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia, which started in the fourth quarter of 2020. In addition, the Loan Agreement contains covenants that our Quarterly Reports on Form 10-Q for the fiscal quarters ending June 30, 2022 and September 30, 2022 and our future Annual Reports on Form 10-K, must not be subject to any qualification as to going concern. Failure to maintain compliance with these or other covenants would result in an event of default under the Loan Agreement, which could result in enforcement action, including acceleration of amounts due under the Loan Agreement. Additionally, the liabilities under the Loan Agreement will be accelerated, subject to certain exceptions, if we are required to repay to Vifor (International) Ltd., or Vifor Pharma, all or a part of the working capital facility established in connection with the Second Amended and Restated Vifor License Agreement that we entered into with Vifor Pharma, in February 2022, or the Vifor Second Amended Agreement, as a result of certain terminations of the Vifor Second Amended Agreement or otherwise.

In the event there is an acceleration of our and certain of our subsidiaries' liabilities under the Loan Agreement as a result of an event of default or otherwise, we may not have sufficient funds or may be unable to arrange for additional financing to repay the liabilities or to make any accelerated payments, and Pharmakon could seek to enforce security interests in the collateral securing the Loan Agreement and our guarantee of the Term Loans, which would have a material adverse effect on our business, financial condition and results of operations.

The Loan Agreement permits voluntary prepayment at any time in whole or in part, subject to prepayment premiums and make-whole premiums prior to certain dates. Upon a change of control, mandatory prepayment provisions require us to prepay the principal amount outstanding, the applicable prepayment premium and make-whole premium and accrued and unpaid interest. In addition, our obligations in connection with the Loan Agreement could have additional significant adverse consequences, including, among other things:

- restricting our activities, including limitations on transferring certain of our assets, engaging in certain transactions, terminating certain agreements, including the Vifor Second Amended Agreement, incurring certain additional indebtedness, creating certain liens, paying dividends or making certain other distributions and investments;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry;
- placing us at a possible competitive disadvantage compared to our competitors who have a smaller amount of debt or competitors with comparable debt at more favorable interest rates; and
- limiting our ability to borrow additional amounts for working capital, capital expenditures, research and development efforts, acquisitions, debt service requirements, execution of our business strategy and other purposes.

Any of these factors could materially and adversely affect our business, financial condition and results of operations.

Our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P. contains various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.

On February 25, 2021, we entered into a royalty interest acquisition agreement, or the Royalty Agreement, with HealthCare Royalty Partners IV, L.P., or HCR, pursuant to which we sold to HCR our right to the to receive royalties and sales milestones for vadadustat, collectively the Royalty Interest Payments, in each case, payable to us under our Collaboration Agreement dated December 11, 2015, or the MTPC Agreement, with Mitsubishi Tanabe Pharma Corporation, or MTPC, subject to an annual maximum "cap" of $13.0 million, or the Annual Cap, and an aggregate maximum "cap" of $150.0 million, or the Aggregate Cap. Under the Royalty Agreement, we are required to comply with various covenants, including obligations to take certain actions, such as actions with respect to the Royalty Interest Payments, the MTPC Agreement, our agreement with MTPC for the commercial supply of vadadustat drug product, and our intellectual property. In addition, the Royalty Agreement includes customary events of default upon the occurrence of enumerated events, including failure to perform certain covenants and the

occurrence of insolvency events. In the event we violate certain covenants and other provisions, we may not receive sales milestones from HCR even if the applicable sales thresholds are met. Upon the occurrence of an event of default, HCR would have the ability to exercise all available remedies in law and equity, which could have a material adverse effect on our financial condition.

Risks Related to Commercialization

If we are unable to maintain or expand sales and marketing capabilities or enter into additional agreements with third parties, we may not be successful in commercializing Auryxia, vadadustat, if approved, or any other product candidates that may be approved.

In order to market any approved product, we intend to continue to invest in sales and marketing, which will require substantial effort and significant management and financial resources. We have built a commercial infrastructure and sales force in the United States for Auryxia, our first commercial product, and while we believe that we can leverage this commercial foundation for vadadustat, if approved, if we are unable to do so successfully this would materially harm our business. Training a sales force to successfully sell and market a new commercial product is expensive and time-consuming and could delay any commercial launch of such product candidate. We may underestimate the size of the sales force required for a successful product launch and we may need to expand our sales force earlier and at a higher cost than we anticipated. If the commercial launch of vadadustat is delayed or does not occur for any reason, including if we do not receive marketing approval in the timeframe we expect, or at all, we may have prematurely or unnecessarily incurred commercialization expenses.

We devote significant effort, in particular, to recruiting individuals with experience in the sales and marketing of pharmaceutical products. Competition for personnel with these skills is significant and retaining qualified personnel with experience in our industry is difficult. Further, the continuing or recurring restrictions placed on recruiting, training and retention by the ongoing COVID-19 pandemic may further exacerbate these conditions and interfere with our ability to find and retain qualified personnel. As a result, we may not be able to retain our existing employees or hire new employees quickly enough to meet our needs. At the same time, we may face high turnover, requiring us to expend time and resources to source, train and integrate new employees.

There are risks involved with maintaining our own sales and marketing capabilities, including the following:

- potential inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- potential inability of sales personnel to obtain access to physicians, including because of restrictions due to COVID-19;
- potential lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- costs and expenses associated with maintaining our own sales and marketing organization.

If we are unable to maintain our own sales and marketing capabilities, we will not be successful in commercializing Auryxia, vadadustat, if approved, and any other product candidate that may be approved.

Furthermore, if we are unable to maintain our arrangements with third parties with respect to sales and marketing, if we are unsuccessful in entering into additional arrangements with third parties to sell and market our products or we are unable to do so on terms that are favorable to us, or if such third parties are unable to carry out their obligations under such arrangements, it will be difficult to successfully commercialize our product and product candidates, including vadadustat, if approved. For example, if in connection with the Vifor Second Amended Agreement, we experience difficulties with Vifor Pharma, or if Vifor Pharma experiences difficulties with other parties to whom it expects to sell vadadustat, if approved, our ability to commercialize vadadustat will be severely hindered and our business operations will be materially harmed.

Our, or our partners', failure to obtain or maintain adequate coverage, pricing and reimbursement for Auryxia, vadadustat, if approved, or any other future approved products, could have a material adverse effect on our or our collaboration partners' ability to sell such approved products profitably and otherwise have a material adverse impact on our business.

Market acceptance and sales of any approved products, including Auryxia and, if approved, vadadustat, depends significantly on the availability of adequate coverage and reimbursement from third party payors and may be affected by existing and future healthcare reform measures. Governmental authorities, third party payors, and PBMs decide which drugs they will cover, as well as establish formularies or implement other mechanisms to manage utilization of products and determine reimbursement levels. We cannot be sure that coverage or adequate reimbursement will be available for Auryxia, vadadustat, if approved, or any of our potential future products. Even if we obtain coverage for an approved product, third party payors may not establish adequate reimbursement amounts, which may reduce the demand for our product and prompt us to have to reduce pricing for the product. If reimbursement is not available or is limited, we may not be able to commercialize certain of our products.

Coverage and reimbursement by a governmental authority, third-party payor or PBM may depend upon a number of factors, including the determination that use of a product is:

- a covered benefit under the health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient; and
- cost effective.

Obtaining coverage and reimbursement approval for a product from a governmental authority, PBM or a third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. In the United States, there are multiple governmental authorities, PBMs and third-party payors with varying coverage and reimbursement levels for pharmaceutical products, and the timing of commencement of reimbursement by a governmental payor is dependent on the assignment of codes via the Healthcare Common Procedural Coding System, which codes are assigned on a quarterly basis. Within Medicare, for oral drugs dispensed by pharmacies and also administered in facilities, coverage and reimbursement may vary depending on the setting. CMS, local Medicare administrative contractors, Medicare Part D plans and/or PBMs operating on behalf of Medicare Part D plans, may have some responsibility for determining the medical necessity of such drugs, and therefore coverage, for different patients. Different reimbursement methodologies may apply, and CMS may have some discretion in interpreting their application in certain settings.

As an oral drug, Auryxia is covered by Medicare only under Part D. However, in September 2018, CMS decided that Auryxia would no longer be covered by Medicare for the treatment of iron deficiency anemia, or IDA, in adult patients with NDD-CKD, or the IDA Indication, or the CMS Decision. While this decision does not impact CMS coverage of the control of serum phosphorus levels in adult patients with DD-CKD, or the Hyperphosphatemia Indication, it requires Part D plan sponsors to impose prior authorization or other steps to ensure that Auryxia is used only for the Hyperphosphatemia Indication. While we believe that the vast majority of the Medicare prescriptions written for Auryxia today are for the Hyperphosphatemia Indication and therefore will continue to be covered by Medicare with prior authorization, the CMS Decision has had and will continue to have an adverse impact on the sales and future growth of Auryxia for the Hyperphosphatemia Indication and the IDA Indication. For example, in the second quarter of 2020, we reduced our short-term and long-term Auryxia revenue forecast, primarily driven by the compounding impact of the CMS Decision. As a result, we recorded an impairment charge of $115.5 million to the Auryxia intangible asset associated with the developed product rights for Auryxia during the three months ended June 30, 2020.

Medicaid reimbursement of drugs varies by state. Private third-party payor reimbursement policies also vary and may or may not be consistent with Medicare reimbursement methodologies. Manufacturers of outpatient prescription drugs may be required to provide discounts or rebates under government healthcare programs or to certain third-party payors in order to obtain coverage of such products.

Additionally, we may be required to enter into contracts with third party payors and/or PBMs offering rebates or discounts on our products in order to obtain favorable formulary status and we may not be able to agree upon commercially reasonable terms with such third party payors or PBMs, or provide data sufficient to obtain favorable coverage and reimbursement for many reasons, including that we may be at a competitive disadvantage relative to companies with more extensive product lines. In addition, third party payors, PBMs and other entities that purchase our products may impose restrictions on our ability to raise prices for our products over time without incurring additional costs. Four distributors, Fresenius Medical Care Rx, McKesson Corporation, Cardinal Health, Inc. and Amerisource Bergen Drug Corporation, in the aggregate, accounted for a significant percentage of our gross accounts receivable as of December 31, 2021. If we are not able to maintain our arrangements with these key distributors on favorable terms, on a timely basis or at all, or if there is any adverse change in one or more of these distributors' business practices or financial condition, it would adversely impact the market opportunity for Auryxia, our product revenues and operating results.

Furthermore, vadadustat was approved in Japan for the treatment of adult patients with anemia due to CKD and is being marketed by MTPC in Japan under the trade name Vafseo™. Pricing and reimbursement strategy is a key component of MTPC's commercialization plans for Vafseo in Japan. If coverage and reimbursement terms change, MTPC may not be able to, or may decide not to, continue commercialization of Vafseo in Japan.

Although we currently believe it is likely that vadadustat, if approved, will be reimbursed using the Transitional Drug Add-on Payment Adjustment, or TDAPA, followed by reimbursement via the bundled reimbursement model, if vadadustat is neither reimbursed under the TDAPA nor the bundled reimbursement model, then patients would access vadadustat through contracts we negotiate with third party payors for reimbursement of vadadustat, which would be subject to the risks and uncertainties described above. Additionally, applying for and obtaining reimbursement under the TDAPA is expected to take several months following approval, which will affect adoption, uptake and product revenue for vadadustat during that time, and if there are

updates to the TDAPA rule that decrease the basis for reimbursement or eligibility criteria during the transition period or if the TDAPA is eliminated, then our profitability may be adversely affected. For example, the Medicare Payment Advisory Commission, or MedPAC, an independent legislative branch advisory body to Congress on issues related to the Medicare program, has recommended that TDAPA not be provided to newly approved drug products considered to fall within "functional categories" for which costs are already accounted for in the bundled reimbursement model, such as for anemia management drugs.

Further, if vadadustat is approved in the United States and included in the fixed reimbursement model for a bundle of dialysis services, or the bundle, we would be required to enter into contracts to supply vadadustat to specific dialysis providers, instead of through distributors, which we believe could be challenging. The dialysis market is unique and is dominated by two providers: DaVita and Fresenius, which account for a vast majority of the dialysis population in the United States. Under the Vifor Second Amended Agreement, we granted Vifor Pharma an exclusive license to sell vadadustat to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by us, to independent dialysis organizations that are members of group purchase organizations, and to certain non-retail specialty pharmacies in the United States, or the Territory. We refer to Fresenius Medical Care North America and its affiliates, these organizations and specialty pharmacies collectively as the "Supply Group". See Note 4 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K for additional information regarding the Vifor Second Amended Agreement. If vadadustat is approved and we are not able to maintain the Vifor Second Amended Agreement or enter into a supply agreement with DaVita or other dialysis clinics, our business may be materially harmed.

Similar to how payor coverage may affect the sales of a product, formulary status within dialysis organizations may affect what products are prescribed within that specific organization. Therefore, if a product is not on a formulary, the prescribers within that organization may be less likely to prescribe that product or may have a difficult time prescribing that product, resulting in less sales. Further, one dialysis organization's determination to add a product to their formulary does not assure that other dialysis organizations will also add the product to theirs. There is always a risk a dialysis organization will not contract with a drug manufacturer for a specific product, resulting in that product not being on that organization's formulary. If any dialysis organization does not add vadadustat, if approved, to the formulary, our business may be materially harmed.

In addition, we may be unable to sell Auryxia or vadadustat, if approved, to dialysis providers on a profitable basis if CMS significantly reduces the level of reimbursement for dialysis services and providers choose to use alternative therapies or look to re-negotiate their contracts with us. Our profitability may also be affected if our costs of production increase faster than increases in reimbursement levels. Adequate coverage and reimbursement of our products by government and private insurance plans are central to patient and provider acceptance of any products for which we receive marketing approval.

Further, in many countries outside the United States, a drug must be approved for reimbursement before it can be marketed or sold in that country. In some cases, the prices that we intend to charge for our products are also subject to approval. Approval by the FDA does not ensure approval by reimbursement authorities outside the United States, and approval by one reimbursement authority outside the United States does not ensure approval by any other reimbursement authorities. However, the failure to obtain reimbursement in one jurisdiction may negatively impact our ability to obtain reimbursement in another jurisdiction. We may not be able to obtain such reimbursement approvals on a timely basis, if at all, and favorable pricing in certain countries depends on a number of factors, some of which are outside of our control.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully than, we do.

The development and commercialization of new drugs is highly competitive and subject to rapid and significant technological change. Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the development and commercialization of Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired. Our objective is to continue to commercialize Auryxia and develop and commercialize new products with superior efficacy, convenience, tolerability and/or safety. In many cases, any approved products that we commercialize will compete with existing, market-leading products.

Auryxia is competing in the hyperphosphatemia market in the United States with other FDA-approved phosphate binders such as Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Sanofi, PhosLo® and Phoslyra® (calcium acetate), marketed by Fresenius Medical Care North America, Fosrenol® (lanthanum carbonate), marketed by Shire Pharmaceuticals Group plc, and Velphoro® (sucroferric oxyhydroxide), marketed by Fresenius Medical Care North America, as well as over-the-counter calcium carbonate products such as TUMS® and metal-based options such as aluminum, lanthanum and magnesium. Most of the phosphate binders listed above are now also available in generic forms. In addition, other agents are in development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) or could otherwise enter the market, including Ardelyx, Inc.'s tenapanor (which is approved in the United States for the treatment of adults with irritable

bowel syndrome with constipation, but for which the FDA issued a complete response letter for with respect to the control of serum phosphorus in adult patients with CKD on dialysis), that may impact the market for Auryxia.

Auryxia is competing in the IDA market in the United States with over-the-counter oral iron, ferrous sulfate, other prescription oral iron formulations, including ferrous gluconate, ferrous fumerate, and polysaccharide iron complex, and intravenous iron formulations, including Feraheme® (ferumoxytol injection), Venofer® (iron sucrose injection), Ferrlicit® (sodium ferric gluconate complex in sucrose injection), Injectafer® (ferric carboxymaltose injection), and Triferic® (ferric pyrophosphate citrate). In addition, other new therapies for the treatment of IDA may impact the market for Auryxia, such as Shield Therapeutics' plc's Feraccru® (ferric maltol), which is available in Europe for the treatment of IDA and Accrufer® (ferric maltol), which was launched in the United States for the treatment of IDA in July 2021.

Furthermore, Auryxia's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than Auryxia. Other companies have product candidates in various stages of preclinical or clinical development to treat diseases and complications of the diseases for which we are marketing Auryxia. In addition, we entered into settlement agreements with each of our ANDA filers pursuant to which we granted licenses to market a generic version of Auryxia in the United States beginning in March 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature, which may impact our business and results of operation.

Drugs that may compete with vadadustat include Epogen® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa) and Eprex® (epoetin alfa), commercialized by Johnson & Johnson in the United States and Europe, respectively, and Mircera® (methoxy PEG-epoetin beta), commercialized by Vifor Pharma in the United States and Roche Holding Ltd. outside of the United States.

We and our partners may also face competition from potential new anemia therapies. There are several other HIF-PH inhibitor product candidates in various stages of development for anemia indications that may be in direct competition with vadadustat if and when they are approved and launched commercially. These candidates are being developed by companies such as FibroGen Inc., or FibroGen, together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, Japan Tobacco International, or JT, GlaxoSmithKline plc, or GSK, and Bayer HealthCare AG, or Bayer.

Furthermore, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable erythropoiesis stimulating agent, or ESA, utilization and thus limit the market potential for vadadustat if they are approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia that may impact the market for anemia-targeted treatment.

In addition, in the United States, FibroGen filed an NDA for its product candidate, roxadustat, with the FDA, but the FDA issued a complete response letter indicating the FDA will not approve the NDA in its present form and requested that an additional clinical trial for roxadustat be conducted prior to resubmission of the NDA or additional response to the FDA's complete response letter. In Europe however, roxadustat is approved for the treatment of anemia in patients with CKD.

In Japan, Vafseo, which is approved for both the DD and NDD indications, competes with roxadustat, daprodustat and enarodustat. Roxadustat is approved for the treatment of anemia due to CKD in patients on dialysis, or DD-CKD, and patients not on dialysis, or NDD-CKD. In addition, daprodustat, GSK's product candidate, and enarodustat, JT's product candidate, are approved in Japan for the treatment of anemia due to CKD. In addition. Bayer HealthCare AG has submitted an NDA for its product candidate for the treatment of renal anemia in Japan. In China, roxadustat has launched for the treatment of anemia of DD-CKD and for the treatment of anemia due to CKD in NDD-CKD patients.

A biosimilar is a biologic product that is approved based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product. The patents for the existing, branded biologic product must expire in a given market before biosimilars may enter that market without risk of being sued for patent infringement. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the existing, branded product was approved under a Biologics License Application, or BLA. The patents for epoetin alfa, an injectable ESA, expired in 2004 in the EU, and the remaining patents expired between 2012 and 2016 in the United States. Because injectable ESAs are biologic products, the introduction of biosimilars into the injectable ESA market in the United States will constitute additional competition for vadadustat if we are able to obtain approval for and commercially launch vadadustat. In the United States, Pfizer's biosimilar version of injectable ESAs, Retacrit® (epoetin alfa-epbx), was approved by the FDA in May 2018 and launched in November 2018 and several biosimilar versions of injectable ESAs are available for sale in the EU.

Many of our potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining marketing approvals, recruiting patients and manufacturing pharmaceutical products. Large and established

companies such as Amgen and Roche, among others, compete in the market for drug products to treat kidney disease. In particular, these companies have greater experience and expertise in conducting preclinical testing and clinical trials, obtaining marketing approvals, manufacturing such products on a broad scale and marketing approved products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and have collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we are developing obsolete. Smaller and other early stage companies may also prove to be significant competitors. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or marketing approval, or discovering, developing and commercializing competitive products, before, or more effectively than, we do. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and operations will suffer.

The commercialization of Riona and Vafseo™ in Japan and our current and potential future efforts with respect to the development and commercialization of our products and product candidates outside of the United States subject us to a variety of risks associated with international operations, which could materially adversely affect our business.

Our Japanese sublicensee, JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona, the trade name for ferric citrate hydrate in Japan, as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and for the treatment of adult patients with IDA in Japan. We also granted Otsuka Pharmaceutical Co. Ltd., or Otsuka, exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted MTPC exclusive rights to commercialize vadadustat, which has been approved and is being marketed by MTPC in Japan under the trade name Vafseo™. In addition, we have conducted and in the future plan to conduct clinical trials outside of the United States for Auryxia, vadadustat and any other product or product candidate that may be in-licensed or acquired. As a result of these and other activities, we are or may become subject to additional risks in developing and commercializing Auryxia and vadadustat outside the United States, including, among others:

- political, regulatory, compliance and economic developments, weakness or instability that could restrict our ability to manufacture, market and sell our products;
- changes in international medical reimbursement policies and programs;
- changes in healthcare policies of foreign jurisdictions;
- trade protection measures, including import or export licensing requirements and tariffs and our compliance therewith;
- our ability to develop or manage relationships with qualified local distributors and trading companies;
- diminished protection of intellectual property in some countries outside of the United States;
- differing labor regulations and business practices;
- compliance with laws, including the U.S. Foreign Corrupt Practices Act, or FCPA, the UK Bribery Act or similar local regulation, the EU General Data Protection Regulation, or GDPR, and tax, employment, immigration and labor laws;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad, including as a result of COVID-19; and
- business interruptions resulting from geopolitical actions, including war and terrorism, global pandemics, or natural disasters including earthquakes, typhoons, floods and fires.

In addition, we receive revenues from royalty payments converted to U.S. dollars based on net sales of Riona and Vafseo™ in Japanese yen. The exchange rates between the Japanese yen on the one hand, and the U.S. dollar, on the other hand, have changed substantially in recent years and may fluctuate substantially in the future. Our results of operations could be adversely affected over time by certain movements in exchange rates, particularly if the Japanese yen depreciates against the U.S. dollar.

Any of these factors may, individually or as a group, have a material adverse effect on our business and results of operations. As and if we continue to expand our commercialization efforts, we may encounter new risks.

Risks Related to Product Development

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and commercialization of vadadustat and any other product candidates.

The risk of failure in drug development is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Preclinical studies and clinical trials are expensive, difficult to design and implement, can take several years to complete, and their outcomes are inherently uncertain. Failure can occur at any time during the process. For example, we are currently conducting a clinical trial to evaluate three times per week oral dosing of vadadustat for dialysis dependent patients with anemia due to chronic kidney disease. If we experience delays in the conduct of this clinical trial or the results are not positive, it could affect the market potential of vadadustat, if approved. Further, the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, interim results of a clinical trial do not necessarily predict final results, and results of Phase 3 clinical trials for one indication may not be predictive of results of Phase 3 clinical trials for another indication. For example, while we announced positive top-line results from $INNO_2VATE$ and vadadustat achieved the primary and key secondary efficacy endpoint in each of the two PRO_2TECT studies, the PRO_2TECT program did not meet the primary major adverse cardiovascular event, or MACE, safety endpoint. Many companies in the biopharmaceutical industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in early stage development, and we may face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. It is impossible to predict when or if any of our product candidates, including vadadustat, will prove effective or safe in humans or will receive marketing approval or on what terms

We may experience numerous unforeseen events during, or as a result of, preclinical development or clinical trials that could delay, prevent or make more challenging our ability to receive or maintain marketing approval or commercialize our product candidates. We may be required to complete additional clinical trials for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, in order to obtain or maintain required regulatory approvals. Our preclinical studies and clinical trials may take longer to complete than currently anticipated, or may be delayed, suspended, required to be repeated, prematurely terminated or may not successfully demonstrate safety and/or efficacy needed to obtain or maintain regulatory approval for a variety of other reasons, such as:

- the costs may be greater than we anticipate;
- the number of patients required for clinical trials may be larger than we anticipate;
- enrollment in our clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third party contractors, such as our CROs, may fail to comply with regulatory requirements, perform effectively, or meet their contractual obligations to us in a timely manner, or at all, or we may fail to communicate effectively or provide the appropriate level of oversight of such third party contractors;
- the supply or quality of our starting materials, drug substance and drug product necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators, independent data monitoring committees, or IDMCs, institutional review boards, or IRBs, safety committees, or ethics committees, may require that we suspend or terminate our clinical trials for various reasons, including noncompliance with regulatory requirements, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using our product candidate, or a finding that the participants are being exposed to unacceptable health risks;
- clinical trials of our product candidates may produce negative or inconclusive results or results that may be interpreted in a manner different than we interpret them, and we may decide, or regulators may require us, to conduct additional clinical trials, repeat a clinical trial or abandon product development programs;
- lack of adequate funding to continue a clinical trial, including unforeseen costs due to enrollment delays, requirements to conduct additional clinical trials or repeat a clinical trial and increased expenses associated with the services of our CROs and other third parties;
- we may fail to initiate, delay of or failure to complete a clinical trial as a result of an Investigational New Drug application, or IND, being placed on clinical hold by the FDA, the EMA, the PMDA, or other regulatory authorities, or for other reasons, such as failure to recruit or enroll suitable patients or patients' failure to return for post-treatment follow up;
- we may determine to change or expand a clinical trial, including after it has begun;
- clinical trial sites and investigators deviating from the clinical protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial, or failure by us or our CROs to communicate effectively or provide the appropriate level of oversight of such clinical sites and investigators;
- there may be an inability, delay, or failure in identifying and maintaining a sufficient number of clinical trial sites, many of which may already be engaged in other clinical programs;

- there may be a delay or failure in reaching agreement with the FDA, the EMA, the PMDA or other regulatory authorities on a clinical trial design upon which we are able to execute;
- there may be a delay or failure in obtaining authorization to commence a clinical trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- there may be delays in reaching, or failure to reach, agreement on acceptable terms with prospective clinical trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- the FDA, the EMA, the PMDA or other regulatory authorities may require us to submit additional data or impose further requirements before permitting us to initiate a clinical trial or during an ongoing clinical trial;
- the FDA, the EMA, the PMDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- third parties with which we work may fail to comply with good practice quality guidelines and regulations, or GXP, including good laboratory practice, good clinical practice, or GCP, and current good manufacturing practice, or cGMP; or
- there may be changes in governmental regulations or administrative actions.

We may be unable to successfully obtain approval of vadadustat or other product candidates, or to successfully complete clinical trials of Auryxia, vadadustat and other product candidates if the results of those trials and studies are not positive or are only modestly positive, or if there are concerns with the profile due to efficacy or safety. For example, the PRO_2TECT program did not meet the primary MACE safety endpoint, and we are remaining cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients. If any of the foregoing occurs, the following may occur:

- regulators may require that we conduct additional clinical trials, repeat clinical trials or conduct other studies beyond those that we currently contemplate;
- we may be delayed in obtaining marketing approval for vadadustat or other product candidates;
- we may not obtain marketing approval for vadadustat or other product candidates at all;
- we may obtain approval for indications or patient populations that are not as broad as intended or desired;
- we may obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for any approved product or inhibit our ability to successfully commercialize any approved product;
- a REMS or FDA-imposed risk management plan that use risk minimization strategies to ensure that the benefits of certain prescription drugs outweigh their risks, may be required;
- we may be subject to additional post-marketing restrictions and/or requirements; or
- the product may be removed from the market after obtaining marketing approval.

The COVID-19 pandemic has resulted in closures of and may continue to impact clinical trial sites on which we rely and will rely for the completion of certain clinical trials and may delay enrollment of certain planned and ongoing clinical trials. In response to the COVID-19 pandemic, the FDA issued guidance on March 18, 2020, and has thereafter updated it, to address and facilitate the conduct of clinical trials during the pandemic. The guidance sets out a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical study report (or as a separate document) contingency measures implemented to manage the study, and any disruption of the study as a result of the pandemic.

Our product development costs may also increase if we experience development delays or delays in receiving the requisite marketing approvals. Our preclinical studies or clinical trials may need to be restructured or may not be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize vadadustat or any other product candidate, including those that may be in-licensed or acquired, or allow our competitors to bring products to market before we do. This could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.

Identifying and qualifying patients to participate in clinical trials is critical to our success. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our clinical trials. Patients may be unwilling to participate in our clinical trials because of concerns about adverse events observed with the product candidate under study, the current standard of care, competitor products and/or other investigational agents, in each case for the same indications and/or similar patient populations. In addition, in the case of clinical trials of any product candidate, patients currently receiving

treatment with the current standard of care or a competitor product may be reluctant to participate in a clinical trial with an investigational drug. Furthermore, COVID-19 resulted in closures of, and may continue to impact, clinical trial sites on which we rely for the conduct of certain clinical trials and COVID-19 pandemic precautions have caused moderate delays in enrolling new clinical trials and may cause delays in enrolling other new clinical trials. Finally, competition for clinical study sites may limit our access to patients appropriate for our clinical trials. As a result, the timeline for recruiting patients and conducting studies may be delayed. These delays could result in increased costs, delays in advancing our development of any product or product candidate, or termination of the clinical trial altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment is affected by many factors, including:

- severity of the disease under investigation;
- design of the study protocol;
- size and nature of the patient population;
- eligibility criteria for, and design of, the study in question;
- perceived risks and benefits of the product or product candidate under study, including as a result of adverse effects observed in similar or competing therapies;
- proximity and availability of clinical study sites for prospective patients;
- availability of competing therapies and clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product or product candidate being studied in relation to available therapies or other product candidates in development;
- efforts to facilitate timely enrollment in clinical trials;
- clinical trial sites and investigators failing to perform effectively; and
- patient referral practices of physicians.

We may not be able to initiate or complete clinical trials in a timely manner, or at all, if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which may delay approval, or result in failure to obtain approval, of our product candidates, which would have a material adverse effect on our business.

Conducting clinical trials outside of the United States makes us subject to additional risks and complexities and we may not complete such trials successfully, in a timely manner, or at all, which could affect our ability to obtain regulatory approvals.

Our ability to successfully initiate, enroll and complete a clinical study in any country outside of the United States is subject to numerous additional risks unique to conducting business in jurisdictions outside the United States, including:

- difficulty in establishing or managing relationships with qualified CROs, physicians and clinical trial sites;
- difficulty in complying with different local standards for the conduct of clinical trials;
- difficulty in complying with various and complex import laws and regulations when shipping drug to certain countries; and
- the potential burden of complying with a variety of laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

Data obtained from studies conducted in the United States may not be accepted by the EMA, the PMDA and other regulatory authorities outside of the United States. Also, certain jurisdictions require data from studies conducted in their country in order to obtain approval in that country.

If we or our collaboration partners have difficulty conducting our clinical trials in jurisdictions outside the United States as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which could have an adverse effect on our business.

Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that may delay or prevent marketing approval or limit their commercial potential.

Undesirable effects caused by, or other undesirable properties of, Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, or competing commercial products or product candidates in development that utilize a common mechanism of action could cause us or regulatory authorities to interrupt, delay or halt clinical trials, could result in a more restrictive label or the delay, denial or withdrawal of marketing approval by the FDA or

other regulatory authorities, and could lead to potential product liability claims. Results of our clinical trials could reveal a high frequency of undesirable effects or unexpected characteristics.

If we or others identify undesirable effects caused by, or other undesirable properties of, Auryxia, vadadustat, or any other product or product candidate, including those that may be in-licensed or acquired, or if known undesirable effects are more frequent or severe than in the past, or if any of the foregoing are perceived to have occurred, either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- our clinical trials may be put on hold;
- patient recruitment could be slowed, and enrolled patients may not want to complete the clinical trial;
- regulatory authorities may require warnings on the label, such as the warning on Auryxia's label regarding iron overload;
- REMS or FDA-imposed risk management plans that use restrictive risk minimization strategies may be required;
- we may decide to, or be required to, send drug warnings or safety alerts to physicians, pharmacists and hospitals (or the FDA or other regulatory authorities may choose to issue such alerts), or we may decide to conduct a product recall or be requested to do so by the FDA or other regulatory authority;
- reformulation of the product, additional non-clinical or clinical trials, restrictive changes in labeling or changes to or re-approvals of manufacturing facilities may be required;
- we may be precluded from pursuing additional development opportunities to enhance the clinical profile of a product within its indicated populations, or studying the product or product candidate in additional indications and populations or in new formulations; and
- we could be investigated by the government or sued and held liable for harm caused to patients, including in class action lawsuits; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining, whether on a restricted basis or at all, marketing approval and, ultimately, market acceptance or penetration of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired. In addition, any of these events could substantially increase our costs, and could significantly impact our ability to successfully commercialize Auryxia, vadadustat or any other product and product candidate, including those that may be in-licensed or acquired, and generate product revenue.

The patient populations treated with Auryxia and potential patient populations for vadadustat, if approved, have CKD, a serious disease that increases the risk of cardiovascular disease including heart attacks and stroke and, in its most severe form, results in, kidney failure and the need for dialysis or kidney transplant. Many patients with CKD are elderly with comorbidities making them susceptible to significant health risks. Therefore, the likelihood of these patients having adverse events, including serious adverse events is high.

With respect to the global $INNO_2VATE$ Phase 3 program, the incidence of treatment emergent adverse events during the *Correction and Conversion* study in vadadustat treated patients was 83.8% and 85.5% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were hypertension (16.2%/ 12.9%) and diarrhea (10.1%/ 9.7%). Serious treatment emergent adverse events were lower in vadadustat treated patients at 49.7% compared to 56.5% for darbepoetin alfa treated patients. The incidence of treatment emergent adverse events during the prevalent dialysis patient study (*Conversion*) in the vadadustat treated patients was 88.3%, and 89.3% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were diarrhea (13.0%/ 10.1%), pneumonia (11.0%/ 9.7%), hypertension (10.6%/ 13.8%), and hyperkalemia (9.0%/ 10.8%). Serious treatment emergent adverse events were slightly lower for vadadustat treated patients at 55.0% and 58.3% for darbepoetin alfa-treated patients. Patients with DD-CKD experienced an increased risk of thromboembolic events compared to darbepoetin alfa with a time to first event HR of 1.20 (95% CI 0.96 - 1.50) driven by thrombosis of vascular access.

With respect to the global PRO_2TECT Phase 3 program, the incidence of treatment emergent adverse events during the erythropoiesis stimulating agent, or ESA,-untreated patients study (*Correction*) in the vadadustat-treated patients was 90.9%, and 91.6% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (34.7%/ 35.2%), hypertension (17.7%/ 22.1.%), hyperkalemia (12.3.%/ 15.6%), urinary tract infection (12.9%/ 12.0%), diarrhea (13.9%/ 10.0%), peripheral oedema (12.5%/ 10.5%), fall (9.6%/ 10%) and nausea (10%/ 8.2%). Serious treatment emergent adverse events were 65.3% for vadadustat-treated patients and 64.5% for darbepoetin alfa-treated patients. The incidence of treatment emergent adverse events during the ESA-treated patients study (*Conversion*) in vadadustat treated patients was 89.1% and 87.7% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (27.5%/ 28.4%), hypertension (14.4%/ 14.8%), urinary tract infection (12.2%/ 14.5%),

diarrhea (13.8.%/ 8.8.%), peripheral oedema (9.9%/ 10.1%) and pneumonia (10.0%/ 9.7%). Serious treatment emergent adverse events were 58.5% for vadadustat-treated patients and 56.6% for darbepoetin alfa-treated patients.

For example, following the completion of our global Phase 3 clinical program for vadadustat, there was a review of hepatic safety across the vadadustat clinical program, which includes 8 completed Phase 2 and 3 studies in NDD-CKD patients, 10 completed Phase 1, 2, and 3 studies, and two ongoing Phase 3b studies in DD-CKD patients, and 18 completed studies in healthy subjects (17 Phase 1 and one Phase 3). This review included a blinded assessment of all hepatic events in the studies by a panel of hepatic experts and analysis by an independent hepatic expert and our team. While hepatocellular injury attributed to vadadustat was reported in less than 1% of patients, there was one case of severe hepatocellular injury with jaundice, and we cannot guarantee that similar events will not happen in the future.

Serious adverse events considered related to vadadustat and any other product candidates could have material adverse consequences on the development and potential approval of such product candidates and our business as a whole. Our understanding of adverse events in prior clinical trials of our product candidates may change as we gather more information, the FDA may not agree with our assessment of adverse events and additional unexpected adverse events may be observed in future clinical trials or in the market.

Any of the above safety data or other occurrences could delay or prevent us from achieving or maintaining marketing approval, harm or prevent sales of Auryxia or, if approved, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, increase our expenses and impair or prevent our ability to successfully commercialize Auryxia, vadadustat or any other products or product candidates.

In addition, any post-marketing clinical trials conducted, if successful, may expand the patient populations treated with Auryxia, vadadustat or any other product we acquire or for which we receive marketing approval, within or outside of their current indications or patient populations, which could result in the identification of previously unknown undesirable effects, increased frequency or severity of known undesirable effects, or result in the identification of unexpected safety signals. In addition, as Auryxia, vadadustat, if approved, and any other products are commercialized, they will be used in significantly larger patient populations, in less rigorously controlled environments and, in some cases, by less experienced and less expert treating practitioners, than in clinical trials, which could result in increased or more serious adverse effects being reported. As a result, regulatory authorities, healthcare practitioners, third party payors or patients may perceive or conclude that the use of Auryxia, vadadustat, if approved, or any other products are associated with serious adverse effects, undermining our commercialization efforts.

Risks Related to Regulatory Approval

We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat or any other product candidate, or we may experience significant delays in doing so, any of which would materially harm our business.

Clinical trials, manufacturing and marketing of any product or product candidate are subject to extensive and rigorous review and regulation by numerous governmental authorities in the United States and other jurisdictions. Before obtaining marketing approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and marketing approval may never be achieved. Of the large number of drugs in development in the United States and in other jurisdictions, only a small percentage successfully complete the FDA's and other jurisdictions' marketing approval processes and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development and commercialization efforts, we may be unable to successfully obtain regulatory approval for, or commercialize vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.

We and Otsuka, our collaboration partner, are not permitted to market vadadustat in the United States until we receive approval from the FDA, in the EU until we receive approval from the EMA, or in any other jurisdiction until the requisite approval from regulatory authorities in such jurisdiction is received. As a condition to receiving marketing approval for vadadustat, we may be required by the FDA, the EMA or other regulatory authorities to conduct additional preclinical studies or clinical trials. We submitted an NDA to the FDA for vadadustat for the treatment of anemia due to CKD in adult dialysis-dependent and non-dialysis dependent patients in March 2021. Our NDA submission was accepted for filing by the FDA in May 2021. The FDA assigned the application standard review and a PDUFA date of March 29, 2022. The FDA has indicated that it is not currently planning to hold an Advisory Committee meeting to discuss the application for vadadustat. Vadadustat may not receive marketing approval at all and, if approved, the scope of approval may not include the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. We remain cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients as vadadustat did not meet the primary safety endpoint of the PRO_2TECT program.

Further, vadadustat and any other product candidate may not receive marketing approval in the United States or the EU even if it is approved in other countries. For example, although vadadustat is approved in Japan for the treatment of anemia due to CKD in DD-CKD and NDD-CKD adult patients, such approval does not guarantee approval in the United States by the FDA or in the EU by the EMA for this indication or at all.

Obtaining marketing approval in the United States and other jurisdictions for any product candidate depends upon numerous factors, many of which are subject to the substantial discretion of the regulatory authorities, including that regulatory agencies may not complete their review processes in a timely manner and, following completion of the review process, may not grant marketing approval or such marketing approval may be limited. Furthermore, approval of a drug does not ensure successful commercialization. For example, on September 23, 2015, the European Commission, or EC, approved Fexeric for the control of hyperphosphatemia in adult patients with CKD. Pursuant to the sunset clause under EU law, the EC's approval of Fexeric in the EU was contingent on, among other things, our commencing marketing of Fexeric within three years; although we successfully negotiated an extension to December 23, 2019, we did not commence marketing Fexeric by such date and therefore the Fexeric approval in the EU has ceased to be valid.

We could face heightened risks with respect to seeking marketing approval in the United Kingdom, or UK, as a result of the recent withdrawal of the UK from the EU, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the EU, the UK withdrew from the EU, effective December 31, 2020. On December 24, 2020, the UK and the EU entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement would prevent us from commercializing vadadustat or any other product candidate, including those that may be in-licensed or acquired, in the UK and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK and/or the EU for vadadustat or any other product candidate, which could significantly and materially harm our business. As of January 1, 2021, the Medicines and Healthcare Products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended) as the basis for regulating medicines.

In addition, the safety concerns associated with the current standard of care for the indications for which we are seeking marketing approval for vadadustat may affect the FDA's, the EMA's or other regulatory authorities' review of the safety results of vadadustat. Additionally, these regulatory authorities may not agree with our assessment of adverse events. Further, the policies or regulations, or the type and amount of clinical data necessary to gain approval, may change during the course of a product candidate's clinical development and may vary among jurisdictions. It is possible that vadadustat will never obtain marketing approval in certain jurisdictions or for some or all of the indications for which we seek approval. The FDA, the EMA or other regulatory authorities may delay, limit or deny approval of vadadustat for many reasons including, among others:

- we may not be able to demonstrate that vadadustat is safe and effective in treating adult patients with anemia due to CKD to the satisfaction of the FDA;
- the results of our clinical trials may only be modestly positive, or there may be concerns with the profile due to efficacy or safety;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA for review and/or marketing approval;
- the FDA may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA may not approve the formulation, labeling or specifications we request for vadadustat;
- the FDA may approve vadadustat or any other product candidate for use only in a small patient population or for fewer or more limited indications than we request;
- the FDA may require that we conduct additional clinical trials or repeat one or more clinical trials;
- the FDA may require development of a REMS as a condition of approval or post-approval;
- the FDA may grant approval contingent on the performance of costly post-marketing clinical trials;
- the FDA's onsite inspections may be delayed due to the COVID-19 pandemic;
- we, or our CROs or other vendors, may fail to comply with GXP or fail to pass any regulatory inspections or audits;
- we or our third party manufacturers may fail to perform in accordance with the FDA's cGMP requirements and guidance;
- the FDA may disagree with inclusion of data obtained from certain regions outside the United States to support the NDA for potential reasons such as differences in clinical practice from United States standards;
- the FDA could deem that our financial relationships with certain principal investigators constitute a conflict of interest, such that the data from those principal investigators may not be used to support our applications;

- although the FDA has indicated that they are not currently planning to hold an Advisory Committee meeting to discuss the NDA for vadadustat, the FDA may ask an Advisory Committee to review portions of the NDA, the FDA may have difficulty scheduling an Advisory Committee meeting in a timely manner or, if convened, an FDA Advisory Committee could recommend non-approval, conditions of approval or restrictions on approval, and the FDA may ultimately agree with the recommendations;
- the FDA's review process and decision-making regarding vadadustat and any other product candidate may be impacted by the results of our and our competitors' clinical trials and safety concerns of marketed products used to treat the same indications as the indications for which vadadustat and any other product candidate are being developed;
- the FDA may not approve the manufacturing processes or facilities of third party manufacturers with whom we contract; or
- the policies or regulations of the FDA may significantly change in a manner that renders our clinical data insufficient for approval, or requires us to amend or submit new clinical protocols.

In addition, similar reasons may cause the EMA or other regulatory authorities to delay, limit or deny approval of vadadustat outside of the United States.

If we experience delays in obtaining approval, or if we fail to obtain approval of vadadustat for some or all of the indications for which we have sought approval, the commercial prospects for vadadustat may be harmed and our ability to generate revenues will be materially impaired, which could have a material adverse effect on our business.

Products approved for marketing are subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties, including withdrawal of marketing approval, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, when and if any of them is approved.

Marketing approvals may be subject to limitations on the approved indicated uses for which the product may be marketed or other conditions of approval, or contain requirements or commitments for potentially costly post-marketing studies and surveillance to monitor the safety and efficacy of the product, including REMS, or registries or observational studies. For example, in connection with the FDA approvals of Auryxia, we initially committed to the FDA to conduct certain post-approval pediatric studies of Auryxia under the Pediatric Research Equity Act of 2003, or PREA. With regard to the Hyperphosphatemia Indication for Auryxia, we committed to completing the post-approval pediatric study and submitting a final report to the FDA by December 31, 2019. With regard to our IDA Indication, we initially committed to completing the post-approval pediatric study and submitting a final report to the FDA by January 2023.With regard to the Hyperphosphatemia Indication, we did not complete and submit the post-marketing requirement pediatric clinical study report by December 31, 2019, and we received a notification of noncompliance with PREA. Our request to extend this deadline was denied, and the study is considered delayed. With regard to the IDA Indication, we did not meet a milestone relating to the post-approval pediatric study of Auryxia in a timely manner and received a notification from the FDA. Subsequently, the FDA agreed to extend the pediatric clinical study timelines for the IDA Indication. We subsequently communicated to the FDA that we would be delaying the start of the clinical trial to produce smaller size tablets. In response, the FDA issued a clinical hold until we manufacture the smaller tablets and provide the FDA with relevant information regarding the smaller sized product for review. If we are unable to complete these studies successfully, we will need to inform the FDA, have further discussions and, if the FDA finds that we failed to comply with pediatric study requirements, it could initiate proceedings to seize or enjoin the sale of Auryxia, which would have a material adverse impact on our ability to commercialize Auryxia and our ability to generate revenues from Auryxia.

In addition, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for Auryxia, vadadustat, if approved, and any other product for which we receive regulatory approval will be subject to extensive and ongoing regulatory requirements and guidance. These requirements and guidance include manufacturing processes and procedures (including record keeping), the implementation and operation of quality systems to control and assure the quality of the product, submissions of safety and other post-marketing information and reports, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. If we, our CMOs or other third parties we engage fail to adhere to such regulatory requirements and guidance, we could suffer significant consequences, including product seizures or recalls, loss of product approval, fines and sanctions, reputational damage, loss of customer confidence, shipment delays, inventory shortages, inventory write-offs and other product-related charges and increased manufacturing costs, and our development or commercialization efforts may be materially harmed.

Moreover, the FDA and other regulatory authorities closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory authorities impose stringent restrictions on companies' communications regarding use of their products, and if we promote any approved product beyond its approved indications or inconsistent with the approved label, we may be subject to enforcement actions or prosecution arising from such activities. Violations of the U.S. Federal Food, Drug,

and Cosmetic Act, or the FDCA, relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse and other laws, as well as state consumer protection laws, insurance fraud laws, third party payor actions, shareholder actions and other lawsuits.

Post-approval discovery of previously unknown problems with an approved product, including adverse events of unanticipated severity or frequency or relating to manufacturing operations or processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing, distribution, use or manufacturing of the product;
- withdrawal of the product from the market, or product recalls;
- restrictions on the labeling or marketing of a product;
- fines, restitution or disgorgement of profits or revenues;
- warning or untitled letters or clinical holds;
- refusal by the FDA or other regulatory authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- REMS; and
- injunctions or the imposition of civil or criminal penalties.

For example, we previously had three limited, voluntary recalls of Auryxia. These and any other recalls or any supply, quality or manufacturing issues in the future could result in significant negative consequences, including reputational harm, loss of customer confidence, and a negative impact on our financials, any of which could have a material adverse effect on our business and results of operations, and may impact our ability to supply Auryxia, Vafseo™, in Japan or vadadustat for commercial and clinical use.

Non-compliance with the FDA, the EMA, the PMDA and other regulatory authorities' requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties.

The FDA's policies and those of other regulatory authorities may change, and additional government regulations may be enacted. We cannot predict the likelihood, nature or extent of government regulations that may arise from future legislation or administrative action, either in the United States or in other jurisdictions. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would materially adversely affect our business.

Risks Related to Governmental Regulation and Compliance

We are subject to a complex regulatory scheme that requires significant resources to ensure compliance and our failure to comply with applicable laws could subject us to government scrutiny or enforcement, potentially resulting in costly investigations, fines, penalties or sanctions, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

In general, a variety of laws apply to us or may otherwise restrict our activities, including, but not limited to, the following:

- laws and regulations governing the conduct of preclinical studies and clinical trials in the United States and other countries in which we are conducting such studies;
- anti-corruption and anti-bribery laws, including the FCPA, the UK Bribery Act and various other anti-corruption laws in countries outside of the United States;
- data privacy laws existing in the United States, the EU and other countries in which we operate, including the U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, the GDPR, and state privacy and data protection laws, such as the California Consumer Privacy Act, or CCPA, as well as state consumer protection laws;
- federal and state laws requiring the submission of accurate product prices and notifications of price increases;
- federal and state securities laws;
- environmental, health and safety laws and regulations; and
- international trade laws, which are laws that regulate the sale, purchase, import, export, re-export, transfer and shipment of goods, products, materials, services and technology.

In addition, our relationships with healthcare providers, physicians and third party payors expose us to broadly applicable fraud and abuse laws that may constrain the business or financial arrangements and relationships through which we market, sell and distribute Auryxia and vadadustat, if approved, and any other products for which we may obtain marketing approval. As such, these arrangements are subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations at federal, state and international levels. These restrictions include, but are not limited to, the following:

- the FDCA which among other things, strictly regulates drug product marketing and promotion and prohibits manufacturers from marketing such products for off-label use;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs, and laws requiring notification of price increases;
- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, and violations of the FDCA, the federal government pricing laws, and the federal Anti-Kickback Statute trigger liability under the federal False Claims Act;
- HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the HITECH, and their respective implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act (renamed the Open Payments Act) requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and other healthcare providers and their immediate family members;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and gift ban and transparency statutes, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by state Medicaid or other programs, or non-governmental third party payors, including private insurers, and which are not preempted by federal laws and often differ from state to state, thus complicating compliance efforts; and
- U.S. state laws restricting interactions with healthcare providers and other members of the healthcare community or requiring pharmaceutical manufacturers to implement certain compliance standards, which vary from state to state.

Because of the breadth of these U.S. laws, and their non-U.S. equivalents, and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent healthcare reforms have strengthened these laws. For example, the Health Care Reform Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate the law. The Health Care Reform Act also amended the False Claims Act, such that violations of the Anti-Kickback Statute are now deemed violations of the False Claims Act.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, such as the Pharmaceutical Research and Manufacturers of America Code on Interactions with Health Care Professionals, known as the PhRMA Code. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA.

Efforts to ensure that our business complies with applicable healthcare laws and regulations involves substantial costs and requires us to expend significant resources. One of the potential areas for governmental scrutiny involves federal and state requirements for pharmaceutical manufacturers to submit accurate price reports to the government. Because our processes for calculating applicable government prices and the judgments involved in making these calculations involve subjective decisions and complex methodologies, these calculations are subject to risk of errors and differing interpretations. In addition, they are subject to review and challenge by the applicable governmental agencies, or potential qui tam complaints, and it is possible that such reviews could result in changes, recalculations, or defense costs that may have adverse legal or financial consequences. It

is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could materially adversely affect our business and would result in increased costs and diversion of management attention and could negatively impact the development, regulatory approval and commercialization of Auryxia or vadadustat, any of which could have a material adverse effect on our business. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government funded healthcare programs.

We will incur significant liability if it is determined that we are promoting any "off-label" use of Auryxia or any other product we may develop, in-license or acquire or if it is determined that any of our activities violates the federal Anti-Kickback Statute.

Physicians are permitted to prescribe drug products for uses that differ from those approved by the FDA or other applicable regulatory agencies. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict manufacturer communications regarding unapproved uses of an approved drug. Companies are not permitted to promote drugs for unapproved uses or in a manner that is inconsistent with the FDA-approved labeling. There are also restrictions about making comparative or superiority claims based on safety or efficacy that are not supported by substantial evidence. Accordingly, we may not promote Auryxia in the United States for use in any indications other than the Hyperphosphatemia Indication and the IDA Indication, and all promotional claims must be consistent with the FDA-approved labeling for Auryxia.

Promoting a drug off-label is a violation of the FDCA and can give rise to liability under the federal False Claims Act, as well as under additional federal and state laws and insurance statutes. The FDA, the Department of Justice and other regulatory and enforcement authorities enforce laws and regulations prohibiting promotion of off-label uses and the promotion of products for which marketing approval has not been obtained, as well as the false advertising or misleading promotion of drugs. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. In addition, laws and regulations govern the distribution and tracing of prescription drugs and prescription drug samples, including the Prescription Drug Marketing Act of 1976 and the Drug Supply Chain Security Act, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level and set minimum standards for the regulation of drug distributors by the states. A company that is found to have improperly promoted off-label uses or to have otherwise engaged in false or misleading promotion or improper distribution of drugs will be subject to significant liability, potentially including civil and administrative remedies as well as criminal sanctions. It may also be subject to exclusion and debarment from federal healthcare reimbursement programs.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. In addition, under some relatively recent guidance from the FDA, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We intend to engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. Although we believe we have put in place a robust compliance program and processes designed to ensure that all such activities are performed in a legal and compliant manner, Auryxia is our first commercial product in the United States, so our implementation of our compliance program in connection with commercialization activities is still relatively new.

In addition, if a company's activities are determined to have violated the federal Anti-Kickback Statute, this can also give rise to liability under the federal False Claims Act and such violations can result in significant fines, criminal and civil remedies, and exclusion from Medicare and Medicaid. There is increased government focus on relationships between the pharmaceutical industry and physicians, pharmacies (especially specialty pharmacies), and other sources of referrals. Common industry activities, such as speaker programs, insurance assistance and support, relationships with foundations providing copayment assistance, and relationships with patient organizations and patients are receiving increased governmental attention. If any of our relationships or activities is determined to violate applicable federal and state anti-kickback laws, false claims laws, or other laws or regulations, the company and/or company executives, employees, and other representatives could be subject to significant fines and criminal sanctions, imprisonment, and potential exclusion from Medicare and Medicaid.

Disruptions in the FDA and other government agencies caused by global health concerns or funding shortages could prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including global health concerns, government budget and funding levels, staffing shortages, statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result of certain of these factors. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may increase the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

In response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. In 2020 and 2021, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. This risk-based assessment system identifies the categories of regulatory activity that can occur within a given geographic area, ranging from critical inspections to resumption of all regulatory activities. In May 2021, the FDA issued a new report "Resiliency Roadmap for FDA Inspectional Oversight" which included its detailed plan to move towards a more consistent state of operations; best-case, base-case and worst-case scenarios are identified, as well as the drivers that determine these scenarios and the impact these will have on inspection activities. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the United States may also impose similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Compliance with privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data when required, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, when required, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third party processors. The GDPR increases our obligations with respect to sponsors with clinical trial sites in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial patients and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the EU. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive

data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar privacy and data security requirements are either in place or underway in the United States. There are a broad variety of data protection laws that may be applicable to our activities, and a range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the CCPA, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by GDPR. Because of this, we may need to engage in additional activities (e.g., data mapping) to identify the personal information we are collecting and the purposes for which such information is collected. In addition, we will need to ensure that our policies recognize the rights granted to consumers (as that phrase is broadly defined in the CCPA and can include business contact information). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with current and any future federal and state laws regarding privacy and security of personal information could expose us to fines and penalties. We also face a threat of potential consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Legislative and regulatory healthcare reform may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain for any products that are approved in the United States or foreign jurisdictions.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of vadadustat, or any other product candidate, restrict or regulate post-approval activities and affect our ability to profitably sell Auryxia and vadadustat, if approved. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA approved product, such as Auryxia or vadadustat, if approved, or any reimbursement that physicians receive for administering any approved product.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for Auryxia and any other approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the ACA. Among the provisions of the ACA of potential importance to our business including, without limitation, our ability to commercialize and the prices we obtain for Auryxia and may obtain for any of our product candidates that are approved for sale, are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal anti-kickback statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes and regulatory have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of 2% per fiscal year. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester, through 2030. The American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, other legislative and regulatory changes have been proposed, but not yet adopted. For example, in July 2019, HHS proposed regulatory changes in kidney health policy and reimbursement. Any new legislative or regulatory changes may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for Auryxia or vadadustat, if approved, or the frequency with which Auryxia and vadadustat, if approved, is prescribed or used.

With the enactment of the Tax Cuts and Jobs Act of 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause an estimated 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. The prior administration also took executive actions to undermine or delay implementation of the ACA. In addition, CMS has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

Further, on December 14, 2018, a United States District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and, therefore, because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On November 10, 2020, the United States Supreme Court heard this case. On June 17, 2021, the Supreme Court dismissed this case after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Accordingly, all of the provisions in the ACA but the individual mandate to buy health insurance remain in effect. It is unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA and our business.

The costs and prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent United States congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Specifically, there have been several recent United States congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

For example, the former administration issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

At the same time, the administration may seek to limit Medicare Part D and public option drug prices through a tax penalty on manufacturers for increases in the cost of drugs and biologics above the general inflation rate. The American Rescue Plan Act of 2021, comprehensive COVID-19 relief legislation recently enacted under the current administration, includes a number of healthcare-related provisions, such as support to rural health care providers, increased tax subsidies for health insurance purchased through insurance exchange marketplaces, financial incentives to states to expand Medicaid programs and elimination of the Medicaid drug rebate cap effective in 2024.

Further, on July 9, 2021, the current administration signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs HHS to create a plan within 45 days to combat “excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging.” On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with

manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products or put pressure on our product pricing.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for Auryxia and any product candidates for which we receive marketing approval or additional pricing pressures. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for Auryxia and any products candidates for which we receive marketing approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain and maintain coverage and reimbursement approval for Auryxia or any other approved product;
- our ability to generate revenues and achieve or maintain profitability; and
- the level of taxes that we are required to pay.

In addition, in some countries, including member states of the EU the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take a significant amount of time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices, and in certain instances render commercialization in certain markets infeasible or disadvantageous from a financial perspective. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product and/or our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third party payors or government authorities may lead to further pressure on the prices or reimbursement levels. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, the commercial launch of our product and/or product candidates could be delayed, possibly for lengthy periods of time, we or our collaborators may not launch at all in a particular country, we may not be able to recoup our investment in one or more product candidates, and there could be a material adverse effect on our business.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the use and disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials by our employees, contractors or consultants, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to our Reliance on Third Parties

We depend on collaborations with third parties for the development and commercialization of Auryxia, Riona, Vafseo and vadadustat and if these collaborations are not successful or if our collaborators terminate their agreements with us, we may not be able to capitalize on the market potential of Auryxia, Riona, Vafseo and vadadustat, and our business could be materially harmed.

We sublicensed the rights to commercialize Riona to JT and Torii in Japan. We entered into collaboration agreements with Otsuka to develop and commercialize vadadustat in the United States, Europe, China and certain other territories. We also entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other Asian countries. In addition, we entered into the Vifor Second Amended Agreement pursuant to which we granted Vifor Pharma an exclusive license to sell vadadustat to the Supply Group in the Territory. We may form or seek other strategic alliances, joint ventures, or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our and our partners' commercialization efforts with respect to Auryxia, Riona, Vafseo and our and our partners' development and commercialization efforts with respect to vadadustat and any other product candidates.

We may not be able to maintain our collaborations for development and commercialization and these collaborations may not be successful due to a number of important factors, including the following:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborations may be terminated in accordance with the terms of the collaboration agreements and, if terminated, may make it difficult for us to attract new collaborators or adversely affect how we are perceived in scientific and financial communities, and may result in a need for additional capital and expansion of our internal capabilities to pursue further development or commercialization of the applicable products and product candidates;
- if permitted by the terms of the collaboration agreements, collaborators may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus, availability of funding or other external factors such as a business combination that diverts resources or creates competing priorities;
- if permitted by the terms of the collaboration agreements, collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- a collaborator with marketing and distribution rights to our products may not commit sufficient resources to their marketing and distribution;
- if permitted by the terms of the collaboration agreements, we and our collaborator may have a difference of opinion regarding the development or commercialization strategy for a particular product or product candidate, and our collaborator may have ultimate decision making authority;
- disputes may arise between a collaborator and us that cause the delay or termination of activities related to research, development or commercialization of Auryxia or vadadustat and any other product candidate, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may not lead to development or commercialization of products and product candidates, if approved, in the most efficient manner or at all;
- a significant change in the senior management team, a change in the financial condition or a change in the business operations, including a change in control or internal corporate restructuring, of any of our collaborators, could result in delayed timelines, re-prioritization of our programs, decreasing resources or funding allocated to support our programs, or termination of the collaborations; and
- collaborators may not comply with all applicable regulatory and legal requirements.

If any of these events occurs, the market potential of Auryxia and vadadustat, if and where approved, and any other products or product candidates, could be reduced, and our business could be materially harmed. We also cannot be certain that, following a collaboration, the benefits of the collaboration will outweigh the potential risks.

We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.

We will require substantial additional cash to fund the continued commercialization of Auryxia and the development and potential commercialization of vadadustat and any other product candidates. We may decide to enter into additional collaborations for the development and commercialization of vadadustat or Auryxia, both within and outside of the United States. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, divert management's attention, or disrupt our business.

We may not be successful in entering into additional collaborations as a result of many factors, including the following:

- competition in seeking appropriate collaborators;
- a reduced number of potential collaborators due to recent business combinations in the pharmaceutical industry;
- an inability to negotiate collaborations on acceptable terms, on a timely basis or at all;
- any international rules, regulations, guidance, laws, risks or uncertainties with respect to potential partners outside of the United States;
- a potential collaborator's evaluation of Auryxia, vadadustat or any other product or product candidate may differ substantially from ours;
- a potential collaborator's resources and expertise; and
- restrictions due to an existing collaboration agreement.

If we are unable to enter into additional collaborations, we may have to delay or curtail the commercialization of Auryxia or vadadustat, if and where approved, reduce or delay its development program or other of our other development programs, or increase our expenditures and undertake additional development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop or commercialize Auryxia or vadadustat, in the case of commercialization, if approved.

Even if we enter into additional collaboration agreements and strategic partnerships or license our intellectual property, we may not be able to maintain them or they may be unsuccessful, which could delay our timelines or otherwise adversely affect our business.

Royalties from commercial sales of vadadustat under our MTPC Agreement will likely fluctuate and will impact our rights to receive future payments under our Royalty Agreement with HCR.

Pursuant to the Royalty Agreement with HCR, we sold to HCR our right to receive the Royalty Interest Payments payable to us under our the MTPC Agreement, subject to the Annual Cap and the Aggregate Cap. After HCR receives Royalty Interest Payments equal to the Annual Cap in a given calendar year, we will receive 85% of the Royalty Interest Payments for the remainder of that year. After HCR receives Royalty Interest Payments equal to the Aggregate Cap, or we pay the Aggregate Cap to HCR (net of the Royalty Interest Payments already received by HCR), the Royalty Interest Payments will revert back to us, and HCR would have no further right to any Royalty Interest Payments. We received $44.8 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and we are eligible to receive up to an additional $15.0 million under the Royalty Agreement if specified sales milestones are achieved for vadadustat in the territory covered by the MTPC Agreement, subject to the satisfaction of certain customary conditions.

The royalty revenues under the MTPC Agreement may fluctuate considerably because they depend upon, among other things, the rate of growth of sales of vadadustat in the territory covered by the MTPC Agreement. Negative fluctuations in these royalty revenues could delay, diminish or eliminate our right to receive up to the additional $15.0 million under the Royalty Agreement upon achievement of the specified sales milestones, our ability to receive 85% of the Royalty Interest Payments after the Annual Cap is achieved in a given calendar year, or our ability to receive 100% of the Royalty Interest Payments after the Aggregate Cap is achieved.

We rely on third parties to conduct all aspects of our product manufacturing and the loss of these manufacturers, their failure to supply us on a timely basis, or at all, or their failure to successfully carry out their contractual duties or comply with regulatory requirements, cGMP requirements, or guidance could cause delays in or disruptions to our supply chain and substantially harm our business.

We do not have any manufacturing facilities and do not expect to independently manufacture any product or product candidates. We currently rely, and expect to continue to rely, on third party manufacturers to produce all of our commercial, clinical and preclinical supply, including the vadadustat drug product that we supply to our collaboration partner, MTPC, for

the Japanese market. Our reliance on third party manufacturers increases the risk that we will not have or be able to maintain sufficient quantities of Auryxia and vadadustat or the ability to obtain such quantities at an acceptable cost or quality, which could delay, prevent or impair our and our partners' development or commercialization efforts.

We currently have two suppliers of Auryxia drug substance, Siegfried Evionnaz SA (two approved sites) and BioVectra Inc. (one approved site), and one supplier of Auryxia drug product, Patheon Inc., or Patheon (three approved sites). We have entered into supply agreements with Esteve Química, S.A. and STA Pharmaceutical Hong Kong Limited, a subsidiary of Wuxi AppTec, or STA, for the commercial manufacture of vadadustat drug substance and Patheon Inc. and STA for the commercial manufacture of vadadustat drug product. If any of the following occurs, we may not have sufficient quantities of Auryxia and/or vadadustat to support our clinical trials, development, commercialization, or obtaining and maintaining marketing approvals, which could materially and adversely impact our business and results of operations:

- we are unsuccessful in implementing additional redundant supply arrangements for commercial quantities of vadadustat or in maintaining our current supply arrangements for commercial quantities of Auryxia and vadadustat;
- our commercial supply arrangements for Auryxia or vadadustat are terminated;
- any of our third party manufacturers is unable to fulfill the terms of their agreements with us, including with respect to quality and quantity, or is unable or unwilling to continue to manufacture on the manufacturing lines included in our regulatory filings; or
- any of our third party manufacturers breaches our supply agreements, does not comply with quality or regulatory requirements and guidance, including cGMP or is subject to regulatory review or ceases its operations for any reason.

If any of our third party manufacturers cannot or do not perform as agreed or expected, including as a result of COVID-19, if they misappropriate our proprietary information, if they terminate their engagements with us, if we terminate our engagements with them, or if there is a significant disagreement, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into agreements with other third party manufacturers, which we may not be able to do in a timely manner or on favorable or reasonable terms, if at all. In some cases, there may be a limited number of qualified replacement manufacturers, or the technical skills or equipment required to manufacture a product or product candidate may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party, or a feasible alternative may not exist. These factors would increase our reliance on our current manufacturers or require us to obtain necessary regulatory approvals and licenses in order to have another third party manufacture Auryxia or vadadustat. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the qualification of a new manufacturer and validation of manufacturing processes would negatively affect our ability to supply clinical trials, obtain and maintain marketing approval, or commercialize or satisfy patient demand for Auryxia and vadadustat, where approved, in a timely manner within budget or at all.

Moreover, issues that may arise in any scale-up and technology transfer and continued commercial scale manufacture of our products may lead to significant delays in our development, marketing approval and commercial timelines and negatively impact our financial performance. For example, a production-related issue resulted in an interruption in the supply of Auryxia in the third and fourth quarters of 2016. This supply interruption negatively impacted Keryx’s revenues in 2016. Although this supply interruption was resolved and we have taken and continue to take actions designed to prevent future interruptions in the supply of Auryxia, any future supply interruptions, whether quality or quantity based, for Auryxia and vadadustat, if and where approved, would negatively and materially impact our reputation and financial condition.

There are a limited number of manufacturers that are capable of manufacturing Auryxia and vadadustat for us and complying with cGMP regulations and guidance and other stringent regulatory requirements and guidance enforced by the FDA, EMA, PMDA and other regulatory authorities. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation, which occur in addition to our own quality assurance releases. The facilities and processes used by our third party manufacturers to manufacture Auryxia may be inspected by the FDA and other regulatory authorities at any time, and the facilities and processes used by our third party manufacturers to manufacture vadadustat will be inspected by the FDA, the EMA and other regulatory authorities prior to or after we submit our marketing applications. Although we have general visibility into the manufacturing processes of our third party manufacturers, we do not ultimately control such manufacturing processes of, and have little control over, our third party manufacturers, including, without limitation, their compliance with cGMP requirements and guidance for the manufacture of certain starting materials, drug substance and finished drug product. Similarly, although we review final production, we have little control over the ability of our third party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Our third party manufacturers may experience problems with their manufacturing and distribution operations and processes, including, for example, quality issues, such as product specification and stability failures, procedural deviations, improper equipment installation or operation, utility failures, contamination, natural disasters and public health epidemics. We may also encounter difficulties relating to our own quality processes and procedures, including regulatory compliance, lot release, quality control and quality assurance, as well as shortages of qualified personnel. If our third party manufacturers cannot successfully

manufacture material that conforms to our specifications and regulatory requirements and guidance, or if we or our third party manufacturers experience manufacturing, operations and/or quality issues, including an inability or unwillingness to continue manufacturing our products at all, in accordance with agreed-upon processes or on currently validated manufacturing lines, we may not be able to supply patient demand or maintain marketing approval for Auryxia or secure and maintain marketing approval for vadadustat.

If the FDA, the EMA or other regulatory authorities do not approve the facilities being used to manufacture vadadustat, or if they withdraw any approval of the facilities being used to manufacture Auryxia or Vafseo™, in Japan, we may need to find alternative manufacturing facilities, which would significantly impact our ability to continue commercializing Auryxia or develop, obtain marketing approval for or market vadadustat or our other product candidates, if approved.

Moreover, our failure or the failure of our third party manufacturers to comply with applicable regulations or guidance, or our failure to oversee or facilitate such compliance, could result in sanctions being imposed on us or our third party manufacturers, including, where applicable, clinical holds, fines, injunctions, civil penalties, delays in, suspension of or withdrawal of approvals, license revocation, seizures or recalls of Auryxia or vadadustat, operating restrictions, receipt of a Form 483 or warning letter, or criminal prosecutions, any of which could significantly and adversely affect the supply of Auryxia or vadadustat. For example, we previously had three limited, voluntary recalls of Auryxia. These and any other recalls or any supply, quality or manufacturing issues in the future and any related write-downs of inventory or other consequences could result in significant negative consequences, including reputational harm, loss of customer confidence, and a negative impact on our financials, any of which could have a material adverse effect on our business and results of operations, and may impact our ability to supply Auryxia, Vafseo in Japan or vadadustat for clinical and commercial use. Also, if our starting materials, drug substance or drug product are damaged or lost while in our or our third party manufacturers' control, it may adversely impact our ability to supply Auryxia or vadadustat, and we may incur significant financial harm.

In addition, Auryxia and vadadustat may compete with other products and product candidates for access to third party manufacturing facilities. A third party manufacturer may also encounter delays or operational issues brought on by sudden internal resource constraints, labor disputes, shifting priorities or shifting regulatory protocols including, in each case, relating to the COVID-19 pandemic. Certain of these third party manufacturing facilities may be contractually prohibited from manufacturing Auryxia or vadadustat due to exclusivity provisions in agreements with our competitors. Any of the foregoing could negatively impact our third party manufacturers' ability to meet our demand, which could adversely impact our ability to supply Auryxia or vadadustat, and we may incur significant financial harm.

Our current and anticipated future dependence on third parties for the manufacture of Auryxia and vadadustat may adversely affect our and our partners' ability to commercialize Auryxia and vadadustat, where approved, on a timely and competitive basis and any future profit margins.

We rely on third parties to conduct our clinical trials and certain of our preclinical studies. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain or maintain marketing approval for Auryxia, vadadustat or any of our product candidates, and our business could be substantially harmed.

We do not have the ability to independently conduct certain preclinical studies and clinical trials. We are currently relying, and expect to continue to rely, on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our current and future preclinical studies and clinical trials. The third parties on whom we rely may fail to perform effectively, or terminate their engagement with us, for a number of reasons, including the following:

- if they experience staffing difficulties;
- if we fail to communicate effectively or provide the appropriate level of oversight;
- if they undergo changes in priorities or corporate structure including as a result of a merger or acquisition or other transaction, or become financially distressed; or
- if they form relationships with other entities, some of which may be our competitors.

If the third parties on whom we rely to conduct our trials fail to adhere to clinical trial protocols or to regulatory requirements, the quantity, quality or accuracy of the data obtained by the third parties may be compromised. We are exposed to risk of fraud or other misconduct by such third parties.

Any of these events could cause our preclinical studies and clinical trials, including post-approval clinical trials, to be extended, delayed, suspended, required to be repeated or terminated, or we may receive untitled warning letters or be the subject of an enforcement action, which could result in our failing to obtain and maintain marketing approval of vadadustat or any other product candidates on a timely basis, or at all, or fail to maintain marketing approval of Auryxia, or any other products, any of which would adversely affect our business operations. In addition, if the third parties on whom we rely fail to perform

effectively or terminate their engagement with us, we may need to enter into alternative arrangements, which could delay, perhaps significantly, the development and commercialization of vadadustat, if approved, or any other product candidates.

Even though we do not directly control the third parties on whom we rely to conduct our preclinical studies and clinical trials and therefore cannot guarantee the satisfactory and timely performance of their obligations to us, we are nevertheless responsible for ensuring that each of our clinical trials and preclinical studies is conducted in accordance with the applicable protocol, legal and regulatory requirements, including GXP requirements, and scientific standards, and our reliance on these third parties, including CROs, will not relieve us of our regulatory responsibilities. If we or any of our CROs, their subcontractors, or clinical or preclinical trial sites fail to comply with applicable GXP requirements, the clinical data generated in our trials may be deemed unreliable or insufficient, our clinical trials could be put on hold, and/or the FDA, the EMA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical and preclinical trials must be conducted with drug product that meets certain specifications and is manufactured under applicable cGMP regulations. These requirements include, among other things, quality control, quality assurance, and the satisfactory maintenance of records and documentation.

We also rely on third parties to store and distribute drug product for our clinical trials. For example, we use third parties to store product at various sites in Europe and the United States to distribute to our clinical trial sites for our ongoing pediatric trials. Any performance failure on the part of our storage or distributor partners could delay clinical development, marketing approval or commercialization, resulting in additional costs and depriving us of potential product revenue.

If the licensor of certain intellectual property relating to Auryxia terminates, modifies or threatens to terminate existing contracts or relationships with us, our business may be materially harmed.

We do not own all of the rights to our product, Auryxia. We have licensed and sublicensed certain rights, patent and otherwise, to Auryxia from a third party, Panion & BF Biotech, Inc., or Panion, who in turn licenses certain rights to Auryxia from one of the inventors of Auryxia. The license agreement with Panion, or the Panion License Agreement, requires us to meet development milestones and imposes development and commercialization due diligence requirements on us. In addition, under the Panion License Agreement, we must pay royalties based on a mid-single digit percentage of net sales of product resulting from the licensed technologies, including Auryxia, and pay the patent filing, prosecution and maintenance costs related to the license. If we do not meet our obligations in a timely manner, or if we otherwise breach the terms of the Panion License Agreement, Panion could terminate the agreement, and we would lose the rights to Auryxia. For example, following announcement of the Merger, Panion notified Keryx in writing that Panion would terminate the Panion License Agreement on November 21, 2018 if Keryx did not cure the breach alleged by Panion, specifically, that Keryx failed to use commercially reasonable best efforts to commercialize Auryxia outside the United States. Keryx disagreed with Panion's claims, and the parties entered discussions to resolve this dispute. On October 24, 2018, prior to the consummation of the Merger, we, Keryx and Panion entered into a letter agreement, or the Panion Letter Agreement, pursuant to which Panion agreed to rescind any and all prior termination threats or notices relating to the Panion License Agreement and waived its rights to terminate the license agreement based on any breach by us of our obligation to use commercially reasonable efforts to commercialize Auryxia outside the United States until the parties executed an amendment to the Panion License Agreement in accordance with the terms of the Panion Letter Agreement, following consummation of the Merger. On April 17, 2019, we and Panion entered into an amendment and restatement of the Panion License Agreement, or the Panion Amended License Agreement, which reflects certain revisions consistent with the terms of the Panion Letter Agreement. See Note 4 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K for additional information regarding the Panion Amended License Agreement. Even though we entered into the Panion Amended License Agreement, there are no assurances that Panion will not allege other breaches of the Panion Amended License Agreement or otherwise attempt to terminate the Panion Amended License Agreement in the future. In addition, if Panion breaches its agreement with the inventor from whom it licenses rights to Auryxia, Panion could lose its license, which could impair or delay our ability to develop and commercialize Auryxia.

From time to time, we may have disagreements with Panion, or Panion may have disagreements with the inventor from whom it licenses rights to Auryxia, regarding the terms of the agreements or ownership of proprietary rights, which could impact the commercialization of Auryxia, could require or result in litigation or arbitration, which would be time-consuming and expensive, could lead to the termination of the Panion Amended License Agreement, or force us to negotiate a revised or new license agreement on terms less favorable than the original. In addition, in the event that the owners and/or licensors of the rights we license were to enter into bankruptcy or similar proceedings, we could potentially lose our rights to Auryxia or our rights could otherwise be adversely affected, which could prevent us from continuing to commercialize Auryxia.

Risks Related to our Intellectual Property

If we are unable to adequately protect our intellectual property, third parties may be able to use our intellectual property, which could adversely affect our ability to compete in the market.

Our commercial success will depend in part on our ability, and the ability of our licensors, to obtain and maintain patent protection on our drug product and technologies, and to successfully defend these patents against third party challenges. We seek to protect our proprietary products and technology by filing patent applications in the United States and certain foreign jurisdictions. The process for obtaining patent protection is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications in a cost effective or timely manner. In addition, we may fail to identify patentable subject matter early enough to obtain patent protection. Further, license agreements with third parties may not allow us to control the preparation, filing and prosecution of patent applications, or the maintenance or enforcement of patents. Such third parties may decide not to enforce such patents or enforce such patents without our involvement. Thus, these patent applications and patents may not, under these circumstances, be prosecuted or enforced in a manner consistent with the best interests of the company.

Our pending patent applications may not issue as patents and may not issue in all countries in which we develop, manufacture or potentially sell our product or in countries where others develop, manufacture and potentially sell products using our technologies. Moreover, our pending patent applications, if issued as patents, may not provide additional protection for our product.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in pharmaceutical and biotechnology patents has emerged to date. Changes in the patent laws or the interpretation of the patent laws in the United States and other jurisdictions may diminish the value of our patents or narrow the scope of our patent protection. Accordingly, the patents we own or license may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative drug products or technologies or design around our patented drug product and technologies which may have an adverse effect on our business. If our competitors prepare and file patent applications in the United States that claim technology also claimed by us, we may have to participate in interference or derivation proceedings in front of the U.S. Patent and Trademark Office, or USPTO, to determine priority of invention, which could result in substantial cost, even if the eventual outcome is favorable to us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that any related patent may expire prior to, or remain in existence for only a short period following, commercialization, which may significantly diminish our ability to exclude others from commercializing products that are similar or identical to ours. The patents we own or license may be challenged or invalidated or may fail to provide us with any competitive advantage. Since we have licensed or sublicensed many patents from third parties, we may not be able to enforce such licensed patents against third party infringers without the cooperation of the patent owner and the licensor, which may not be forthcoming. In addition, we may not be successful or timely in obtaining any patents for which we submit applications.

Generally, the first to file a patent application is entitled to the patent if all other requirements of patentability are met. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Since publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Moreover, the laws enacted by the Leahy-Smith America Invents Act of 2011, or the Act, which reformed certain patent laws in the United States, introduce procedures that permit competitors to challenge our patents in the USPTO after grant, including inter partes review and post grant review. Similar laws exist outside of the United States. The laws of the European Patent Convention, for example, provide for post-grant opposition procedures that permit competitors to challenge, or oppose, our European patents administratively at the European Patent Office.

In July 2011, a third party filed an opposition to our issued European patents, European Patent No. 2044005, or the ’005 EP Patent, which covers vadadustat. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office decided to maintain certain claims of the patent directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases including, but not limited to, anemia. Both parties appealed the decision of the Opposition Division. On February 27, 2018, we withdrew the ’005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia. We cannot be assured that such claims in the divisional application will be granted by the European Patent Office. If such claims are not granted, or the scope of the claims is significantly narrowed, we may not be able to adequately protect our rights, provide sufficient exclusivity, or preserve our competitive advantage.

We may become involved in addressing patentability objections based on third party submission of references, or we may become involved in defending our patent rights in oppositions, derivation proceedings, reexamination, inter partes review, post grant review, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere,

challenging our patent rights or the patent rights of others. An adverse result in any such proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged on such a basis in the courts or patent offices in the United States and abroad. As a result of such challenges, we may lose exclusivity or freedom-to-operate or patent claims may be narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to prevent third parties from using or commercializing similar or identical products, or limit the duration of the patent protection for our products.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and governmental patent agencies in other jurisdictions also require compliance with a number of procedural, documentary, fee payment (such as annuities) and other similar provisions during the patent application process. While an inadvertent lapse in many cases can be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market sooner than we expect, which would have a material adverse effect on our business.

In addition, patents protecting our product candidate might expire before or shortly after such candidate is commercialized. Thus, our patent portfolio may not provide sufficient rights to exclude others from commercializing products similar or identical to ours.

We also rely on trade secrets and know-how to protect our intellectual property where we believe patent protection is not appropriate or obtainable. Trade secrets are difficult to protect. While we require our employees, licensees, collaborators and consultants to enter into confidentiality agreements, this may not be sufficient to adequately protect our trade secrets or other proprietary information. In addition, in some cases, we share certain ownership and publication rights to data relating to some of our products and product candidates with research collaborators, licensees and other third parties. If we cannot maintain the confidentiality of this information, our ability to receive patent protection or protect our trade secrets or other proprietary information will be at risk.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our products and product candidates in all countries throughout the world would be prohibitively expensive. Consequently, the breadth of our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. As a result, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other countries. Competitors may use our technologies in countries where we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories where we have patent protection, but where enforcement is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop the infringement of our patents or the marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in countries outside of the United States could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage for our products and product candidates from the intellectual property that we develop or license.

The intellectual property that we own or have licensed and related non-patent exclusivity relating to our current and future products is, and may be, limited, which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia.

The patent rights and related non-patent exclusivity that we own or have licensed relating to Auryxia are limited in ways that may affect our ability to exclude third parties from competing against us. For example, a third party may design around our owned or licensed composition of matter patent claims or market a product for the methods of use not covered by our owned or licensed patents.

Obtaining proof of direct infringement by a competitor for a method of use patent requires us to demonstrate that the competitors make and market a product for the patented use(s). Alternatively, we can prove that our competitors induce or contribute to others in engaging in direct infringement. Proving that a competitor contributes to or induces infringement of a patented method by another has additional proof requirements. For example, proving inducement of infringement requires proof of intent by the competitor. If we are required to defend ourselves against claims or to protect our own proprietary rights against others, it could result in substantial costs to us and the distraction of our management. An adverse ruling in any litigation or administrative proceeding could prevent us from marketing and selling Auryxia, increase the risk that a generic or other similar version of Auryxia could enter the market to compete with Auryxia, limit our development and commercialization of Auryxia, or otherwise harm our competitive position and result in additional significant costs.

Moreover, physicians may prescribe a competitive identical product for indications other than the one for which the product has been approved, or “off-label” indications, that are covered by the applicable patents. Although such off-label prescriptions may directly infringe or contribute to or induce infringement of method of use patents, such infringement is difficult to prevent.

In addition, any limitations of our patent protection described above may adversely affect the value of our drug product and may inhibit our ability to obtain a collaboration partner at terms acceptable to us, if at all.

In the United States, the FDA has the authority to grant additional regulatory exclusivity protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity may provide an additional six months which are added to the term of any non-patent exclusivity that has been awarded as well as to the regulatory protection related to the term of a relevant patent, to the extent these protections have not already expired.

In addition to pediatric exclusivity protection, we may seek additional non-patent exclusivity for vadadustat and other product candidates under other provisions of the FDCA such as new chemical entity, or NCE, exclusivity, or exclusivity for a new use or new formulation, but there is no guarantee that vadadustat or any other product candidates will receive such exclusivity. The FDCA provides a five-year period of non-patent exclusivity within the United States to the first applicant to gain approval of an NDA for an NCE. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which consists of the molecule(s) or ion(s) responsible for the action of the drug substance (but not including those portions of the molecule that cause it to be a salt or ester or which are not bound to the molecule by covalent or similar bonds). During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an ANDA or 505(b)(2).

NDA that references an NDA product with NCE exclusivity may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of exclusivity for an NDA, particularly a 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application (for example, for new indications, dosages, or strengths of an existing drug). This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. The three-year exclusivity period, unlike five-year exclusivity, does not prevent the submission of a competing ANDA or 505(b)(2) NDA. Instead, it only prevents the FDA from granting final approval to such a product until expiration of the exclusivity period. Five-year and three-year exclusivity will not delay the submission (in the case of five-year exclusivity) or the approval (in the case of three-year exclusivity) of a full NDA submitted under section 505(b)(1) of the FDCA; however, an applicant submitting a full NDA would be required to conduct all of its own studies needed to independently support a finding of safety and effectiveness for the proposed product, or have a full right of reference to all studies not conducted by the applicant.

We received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg iron per tablet), with the first received on October 31, 2018. We filed certain complaints for patent infringement relating to such ANDAs, and have entered into settlement and license agreements with each of the ANDA filers. See Part I, Item 3. Legal Proceedings for further information relating to the ANDAs, lawsuits and settlements.

In cases where NCE exclusivity has been granted to a new drug product, the 30-month stay triggered by such litigation is extended by the amount of time such that seven years and six months will elapse from the date of approval of the NDA for that product. Without NCE exclusivity, the 30-month stay on FDA final approval of an ANDA runs from the date on which the sponsor of the reference listed drug receives notice of a Paragraph IV certification from the ANDA applicant.

We cannot assure you that Auryxia, vadadustat, if approved, or any of our potential future products will obtain such pediatric exclusivity, NCE exclusivity or any other market exclusivity in the United States, EU or any other territory, or that we will be the first to receive the respective regulatory approval for such drugs so as to be eligible for any non-patent exclusivity protection. We also cannot assure you that Auryxia, vadadustat, if approved, or any of our potential future products will obtain patent term extension.

The market entry of one or more generic competitors or any third party's attempt to challenge our intellectual property rights will likely limit Auryxia sales and have an adverse impact on our business and results of operation.

Although the composition and use of Auryxia is currently claimed by 15 issued patents that are listed in the FDA's Orange Book, we cannot assure you that we will be successful in defending against third parties attempting to invalidate or design around our patents or assert that our patents are invalid or otherwise unenforceable or not infringed, or in competing against third parties introducing generic equivalents of Auryxia or any of our potential future products. If our Orange Book-listed patents are successfully challenged by a third party and a generic version of Auryxia is approved and launched, revenue from Auryxia could decline significantly, which would have a material adverse effect on our sales, results of operations and financial condition.

We previously received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). We filed complaints for patent infringement relating to such ANDAs, and subsequently entered into settlement and license agreements with all such ANDA filers to date See Part I, Item 3. Legal Proceedings for further information relating to the ANDAs, lawsuits and settlements. It is possible that we may receive Paragraph IV certification notice letters from additional ANDA filers, and may not ultimately be successful in an ANDA litigation. Generic competition for Auryxia or any of our potential future products could have a material adverse effect on our sales, results of operations and financial condition.

Litigation, including third party claims of intellectual property infringement, may be costly and time consuming and may delay or harm our drug discovery, development and commercialization efforts.

We may be forced to initiate litigation to enforce our contractual and intellectual property rights, or we may be sued by third parties asserting claims based on contract, tort or intellectual property infringement. In addition, third parties may have or may obtain patents in the future and claim that our products or other technologies infringe their patents. If we are required to defend against suits brought by third parties, or if we sue third parties to protect our rights, we may be required to pay substantial litigation costs, and our management's attention may be diverted from operating our business. In addition, any legal action against our licensor, licensees or us that seeks damages or an injunction of commercial activities relating to Auryxia, vadadustat or any other product candidates or other technologies, including those that may be in-licensed or acquired, could subject us to monetary liability, a temporary or permanent injunction preventing the development, marketing and sale of such products or such technologies, and/or require our licensor, licensees or us to obtain a license to continue to use such products or other technologies. We cannot predict whether our licensor, licensees or we would prevail in any of these types of actions or that any required license would be made available on commercially acceptable terms, if at all.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. The pharmaceutical and biotechnology industries are characterized by extensive litigation over patent and other intellectual property rights. We have in the past and may in the future become a party to, or be threatened with, future adversarial litigation or other proceedings regarding intellectual property rights with respect to our product and product candidates. As the pharmaceutical and biotechnology industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others.

While our product candidates are in preclinical studies and clinical trials, we believe that the use of our product candidates in these preclinical studies and clinical trials in the United States falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e), which provides that it shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention solely for uses reasonably related to the development and submission of information to the FDA. As a result of the Merger, our portfolio includes a commercial product, Auryxia. Also, vadadustat, if approved, could be commercialized in the near future. Consequently, there is an increased possibility of a patent infringement claim against us. We attempt to ensure that our products and product candidates and the methods we employ to manufacture them, as well as the methods for their use which we intend to promote, do not infringe other parties' patents and other proprietary rights. There can be no assurance they do not, however, and competitors or other parties may assert that we infringe their proprietary rights in any event.

FibroGen has filed patent applications in the United States and other countries directed to purportedly new methods of using previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions, and some of

these applications have since issued as patents. To the extent any such patents issue or have been issued, we may initiate opposition or other legal proceedings with respect to such patents. We discuss the status of the opposition and/or invalidation proceedings against certain FibroGen patents in Part I, Item 3. Legal Proceedings of this Annual Report on Form 10-K.

There may be patents of third parties of which we are currently unaware with claims to compounds, materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Also, because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe.

Third parties, including FibroGen, may in the future claim that our product and product candidates and other technologies infringe upon their patents and may challenge our ability to commercialize Auryxia and vadadustat, if approved. Parties making claims against us or our licensees may seek and obtain injunctive or other equitable relief, which could effectively block our or their ability to continue to commercialize Auryxia or further develop and commercialize vadadustat or any other product candidates, including those that may be in-licensed or acquired. If any third party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our products or product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product or product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or our intended methods of use, the holders of any such patent may be able to block or impair our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. We may also elect to enter into a license in order to settle litigation or in order to resolve disputes prior to litigation. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our products or product candidates. Should a license to a third party patent become necessary, we cannot predict whether we would be able to obtain a license or, if a license were available, whether it would be available on commercially reasonable terms. If such a license is necessary and a license under the applicable patent is unavailable on commercially reasonable terms, or at all, our ability to commercialize our product or product candidate may be impaired or delayed, which could in turn significantly harm our business.

Further, defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties or redesign our products, which may be impossible or require substantial time and monetary expenditure.

We are currently involved in a declaratory judgment of non-infringement and invalidity lawsuit, opposition and invalidation proceedings, and may in the future be involved in additional lawsuits or administrative proceedings to challenge the patents of our competitors or to protect or enforce our patents, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or misappropriate our trade secrets or confidential information. To counter infringement or unauthorized use, we may be required to file infringement or misappropriation claims, which can be expensive and time-consuming. We may not be able to prevent infringement of our patents or misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and held not infringed and could put our patent applications at risk of not issuing.

In addition, there may be a challenge or dispute regarding inventorship or ownership of patents or applications currently identified as being owned by or licensed to us. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Interference proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications.

Various administrative proceedings are also available for challenging patents, including interference, reexamination, inter partes review, and post-grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. An unfavorable outcome in any current or future proceeding in which we are challenging third party patents could require us to cease using the patented technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all. Even if we are successful, participation in interference or other administrative proceedings before the USPTO or a foreign patent office may result in substantial costs and distract our management and other employees.

We are involved in an action against our competitors in the federal district court to obtain a declaratory judgment of non-infringement and invalidity of certain patents of the competitors. In addition, we are currently involved in opposition and invalidation proceedings in the European Patent Office, the Japan Patent Office, and the Patents Court of the UK. These proceedings may be ongoing for a number of years and may involve substantial expense and diversion of employee resources from our business. In addition, we may become involved in additional opposition proceedings or other legal or administrative proceedings in the future. For more information, see the other risk factors under "Risks Related to our Intellectual Property".

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation and some administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure during discovery. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from potential collaborators, prospective licensees and other third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

Risks Related to our Business and Managing Growth

If we fail to attract, retain and motivate senior management and qualified personnel, we may be unable to successfully develop, obtain and/or maintain marketing approval of and commercialize vadadustat or commercialize Auryxia.

Recruiting and retaining qualified personnel is critical to our success. We are also highly dependent on our executives, certain members of our senior management and certain members of our commercial organization. The loss of the services of our executives, senior managers or other employees could impede the achievement of our research, development, regulatory and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Losing key personnel subjects us to a number of risks, including the failure to coordinate responsibilities and tasks, the necessity to create new management systems and processes, the impact on corporate culture, and the retention of historical knowledge. Furthermore, replacing executives, senior managers and other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, obtain and/or maintain marketing approval of and commercialize Auryxia, vadadustat and other product candidates. Our future financial performance and our ability to develop, obtain and/or maintain market approval of and commercialize Auryxia and vadadustat and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to hire, train, integrate, and retain additional qualified personnel with sufficient experience. We may be unable to hire, train, retain or motivate these personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel, particularly in our geographic region.

We also experience competition for the hiring of personnel from universities and research institutions. In addition, we rely on contractors, consultants and advisors, including scientific and clinical advisors, to assist us in formulating and executing our research and development and commercialization strategy. Our contractors, consultants and advisors may become employed by companies other than ours and may have commitments with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to grow and pursue our business strategy will be limited.

We may encounter difficulties in managing our growth, including with respect to our employee base, and expanding our operations successfully.

As we commercialize Auryxia and advance vadadustat through development and, if approved, commercialization, we have expanded and may need to further expand our capabilities or contract with third parties to provide these capabilities for us. We may encounter difficulties in managing the size of our operations as well as challenges associated with managing an increasingly diversified business.

We have strategic collaborations for the commercialization of Riona and the development and commercialization of vadadustat, which is now being marketed under the trade name Vafseo™ by our collaboration partner, MTPC, in Japan. Additionally, in the United States, we have strategic relationships with Vifor Pharma and Otsuka related to the commercialization of vadadustat, if approved. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, consultants, vendors, suppliers and other third parties. These relationships are complex and create numerous risks as we deal with issues that arise.

Our future financial performance and our ability to commercialize Auryxia and vadadustat, if and where approved, and to compete effectively will depend, in part, on our ability to manage any future growth effectively. This future growth will impose significant added responsibilities on the business and members of management. To manage our recent and anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, procedures and processes. We may not be able to implement these improvements in an efficient or timely manner and may discover deficiencies in existing systems, procedures and processes. Moreover, the systems, procedures and processes currently in place or to be implemented may not be adequate for such growth. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

In addition, we have experienced and may continue to experience significant growth in our employee base. This growth to date has imposed, and future growth or attrition will continue to impose, significant added responsibilities on members of management, including the need to recruit, hire, retain, motivate and integrate additional employees, including employees who joined us since the COVID-19 pandemic. Due to our limited financial resources, along with the competitive landscape for talent acquisition and retention in the biopharmaceutical industry, we may not be able to effectively manage the expansion of our operations or recruit, train, and retain additional qualified personnel. In addition, we may need to adjust the size of our workforce as a result of changes to our expectations for our business, including as a result of the FDA's decision with respect to approval of vadadustat for DD-CKD and NDD-CKD, which can result in management being required to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth-related activities and related expenses.

We have identified a material weakness in our internal control over financial reporting relating to our inventory process. If we are not able to remediate this material weakness, or if we experience additional material weaknesses or other deficiencies in the future or otherwise fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to maintain or implement required new or improved controls, or difficulties encountered in implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us, as and when required, conducted in connection with Section 404 of the Sarbanes-Oxley Act, or Section 404, or any testing by our independent registered public accounting firm, which became required for us as of December 31, 2019, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. As of December 31, 2019, management and our independent registered public accounting firm concluded that our internal control over financial reporting relating to our inventory process was not effective because of a material weakness due to our failure to design and maintain effective controls over the completeness, accuracy and presentation and disclosure of inventory. Despite remediation efforts we undertook during fiscal 2020 and 2021 and continue to make, our management and independent registered public accounting firm concluded that, as of December 31, 2021, our internal control over financial reporting relating to our inventory process was not effective because we did not maintain effective controls related to the review of inventory reconciliations, the validation of the inventory costing, the periodic assessment of excess and obsolete inventory related reserves and verification that the existence of all inventories subject to physical inventory counts were correctly counted. Additionally, as revised and enhanced controls need to be in operation for a sufficient period of time and be tested to ensure that the controls are operating as designed, management has concluded that the material weakness cannot be considered remediated as of December 31, 2021. Although we have initiated remediation measures to address the material weakness, we cannot provide assurance that we will be able to correct this material weakness in a timely manner or that our remediation efforts will be adequate to allow us to conclude that our internal controls will be effective in the future. Even if this material weakness is remediated in the future, our internal control over financial reporting could in the future have additional material weaknesses, deficiencies or conditions that could require correction or remediation.

We will need to continue to dedicate internal resources, engage outside consultants and maintain a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to remediate the material weakness relating to our inventory process described above and any future control deficiencies or material weaknesses, and improve control processes as appropriate, validate through testing that controls are functioning as documented and maintain a continuous

reporting and improvement process for internal control over financial reporting. If we are not able to correct material weaknesses or deficiencies in internal controls in a timely manner or otherwise comply with the requirements of Section 404 in a timely manner, our ability to record, process, summarize and report financial information accurately and within applicable time periods may be adversely affected and we could be subject to sanctions or investigations by the SEC, the Nasdaq Stock Market or other regulatory authorities as well as shareholder litigation which would require additional financial and management resources and could adversely affect the market price of our common stock. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

Security breaches and unauthorized use of our information technology systems and information, or the information technology systems or information in the possession of our collaborators and other third parties, could damage the integrity of our clinical trials, impact our regulatory filings, compromise our ability to protect our intellectual property, and subject us to regulatory actions that could result in significant fines or other penalties.

We, our collaborators, contractors and other third parties rely significantly upon information technology, and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively. In addition, we and our collaborators, contractors and other third parties rely on information technology networks and systems, including the Internet, to process, transmit and store clinical trial data, patient information, and other electronic information, and manage or support a variety of business processes, including operational and financial transactions and records, personal identifying information, payroll data and workforce scheduling information. We purchase some of our information technology from vendors, on whom our systems depend. We rely on commercially available systems, software, tools and monitoring to provide security for the processing, transmission and storage of company and customer information.

In the ordinary course of our business, we and our third party contractors maintain personal and other sensitive data on our and their respective networks, including our intellectual property and proprietary or confidential business information relating to our business and that of our clinical trial patients and business partners. In particular, we rely on CROs and other third parties to store and manage information from our clinical trials. We also rely on third parties to manage patient information for Auryxia. The secure maintenance of this sensitive information is critical to our business and reputation.

Companies and other entities and individuals have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access to systems and information. These threats can come from a variety of sources, ranging in sophistication from individual hackers to state-sponsored attacks. Cyber threats may be broadly targeted, or they may be custom-crafted against our information systems or those of our vendors or third party service providers. A security breach, cyberattack or unauthorized access of our clinical data or other data could damage the integrity of our clinical trials, impact our regulatory filings, cause significant risk to our business, compromise our ability to protect our intellectual property, and subject us to regulatory actions, including under the GDPR and CCPA discussed elsewhere in these risk factors and the privacy or security rules under federal, state, or other local laws outside of the United States protecting confidential or personal information, that could be expensive to defend and could result in significant fines or other penalties. Cyberattacks can include malware, computer viruses, hacking or other unauthorized access or other significant compromise of our computer, communications and related systems. Although we take steps to manage and avoid these risks and to be prepared to respond to attacks, our preventive and any remedial actions may not be successful and no such measures can eliminate the possibility of the systems' improper functioning or the improper access or disclosure of confidential or personally identifiable information such as in the event of cyberattacks. Security breaches, whether through physical or electronic break-ins, computer viruses, ransomware, impersonation of authorized users, attacks by hackers or other means, can create system disruptions or shutdowns or the unauthorized disclosure of confidential information.

Although we believe our collaborators, vendors and service providers, such as our CROs, take steps to manage and avoid information security risks and respond to attacks, we may be adversely affected by attacks against our collaborators, vendors or service providers, and we may not have adequate contractual remedies against such collaborators, vendors and service providers to remedy any harm to our business caused by such event. Additionally, outside parties may attempt to fraudulently induce employees, collaborators, or other contractors to disclose sensitive information or take other actions, including making fraudulent payments or downloading malware, by using "spoofing" and "phishing" emails or other types of attacks. Our employees may be targeted by such fraudulent activities. Outside parties may also subject us to distributed denial of services attacks or introduce viruses or other malware through "trojan horse" programs to our users' computers in order to gain access to our systems and the data stored therein. In the recent past, cyber-attacks have become more prevalent and much harder to detect and defend against and, because the techniques used to obtain unauthorized access, disable or degrade service, or sabotage systems change frequently and continuously become more sophisticated, often are not recognized until launched against a target and may be difficult to detect for a long time, we may be unable to anticipate these techniques or to implement adequate preventive or detective measures, and we might not immediately detect such incidents and the damage caused by such incidents.

Such attacks, whether successful or unsuccessful, or other compromises with respect to our information security and the measures we implement to prevent, detect and respond to them, could:

- result in our incurring significant costs related to, for example, rebuilding internal systems, defending against litigation, responding to regulatory inquiries or actions, paying damages or fines, or taking other remedial steps with respect to third parties;
- lead to public exposure of personal information of participants in our clinical trials, Auryxia patients and others;
- damage the integrity of our studies or delay their completion, disrupt our development programs, our business operations and commercialization efforts;
- compromise our ability to protect our trade secrets and proprietary information;
- damage our reputation and deter business partners from working with us; or
- divert the attention of our management and key information technology resources.

Any failure to maintain proper functionality and security of our internal computer and information systems could result in a loss of, or damage to, our data or marketing applications or inappropriate disclosure of confidential or proprietary information, interrupt our operations, damage our reputation, subject us to liability claims or regulatory penalties, under a variety of federal, state or other applicable privacy laws, such as HIPAA, the GDPR, or state data protection laws including the CCPA, harm our competitive position and delay the further development and commercialization of our products and product candidates, or impact our relationships with customers and patients.

Our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate applicable laws, including the following:

- FDA and other healthcare authorities' regulations, including those laws that require the reporting of true, complete and accurate information to regulatory authorities, and those prohibiting the promotion of unapproved drugs or approved drugs for an unapproved use;
- quality standards, including GXP;
- federal and state healthcare fraud and abuse laws and regulations and their non-U.S. equivalents;
- anti-bribery and anti-corruption laws, such as the FCPA and the UK Bribery Act or country-specific anti-bribery or anti-corruption laws, as well as various import and export laws and regulations;
- laws that require the reporting of true and accurate financial information and data; and
- U.S. state and federal securities laws and regulations and their non-U.S. equivalents, including those related to insider trading.

We conducted our global clinical trials for vadadustat, and are initiating pediatric trials, in countries where corruption is prevalent, and violations of any of these laws by our personnel or by any of our vendors or agents, such as our CROs or CMOs, could have a material adverse impact on our clinical trials and our business and could result in criminal or civil fines and sanctions. We are subject to complex laws that govern our international business practices. These laws include the FCPA, which prohibits United States companies and their intermediaries, such as CROs or CMOs, from making improper payments to foreign government officials for the purpose of obtaining or keeping business or obtaining any kind of advantage for the company. The FCPA also requires companies to keep accurate books and records and maintain adequate accounting controls. A number of past and recent FCPA investigations by the Department of Justice and the U.S. Securities and Exchange Commission, or the SEC, have focused on the life sciences sector.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. Some of the countries in which we are conducting clinical trials have a history of corruption, which increases our risks of FCPA violations. In addition, the FCPA presents unique challenges in the pharmaceutical industry because in many countries' hospitals are operated by the government, and doctors and other hospital employees are considered foreign government officials. Certain payments made by pharmaceutical companies, or on their behalf by CROs, to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Additionally, the UK Bribery Act applies to our global activities and prohibits bribery of private individuals as well as public officials. The UK Bribery Act prohibits both the offering and accepting a bribe and imposes strict liability on companies for failing to prevent bribery, unless the company can show that it had "adequate procedures" in place to prevent bribery. There are also local anti-bribery and anti-corruption laws in countries where we are conducting clinical trials, and many of these also carry the risk of significant financial or criminal penalties.

We are also subject to trade control regulations and trade sanctions laws that restrict the movement of certain goods, currency, products, materials, services and technology to, and certain operations in, various countries or with certain persons. Our ability to transfer other clinical trial supplies, and for our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors ability to travel, between certain countries is subject to maintaining required licenses and complying with these laws and regulations.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other United States federal and state laws, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us.

The internal controls, policies and procedures, and training and compliance programs we have implemented to deter prohibited practices may not be effective in preventing our employees, contractors, consultants, agents or other representatives from violating or circumventing such internal policies or violating applicable laws and regulations. The failure to comply with laws governing international business practices may impact our clinical trials, result in substantial civil or criminal penalties for us and any such individuals, including imprisonment, suspension or debarment from government contracting, withdrawal of our products, if approved, from the market, or being delisted from The Nasdaq Global Market. In addition, we may incur significant costs in implementing sufficient systems, controls and processes to ensure compliance with the aforementioned laws. The laws and regulations referenced above may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements that could adversely affect our business.

Additionally, it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling known or unknown risks or preventing losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, or if any such action is instituted against our employees, consultants, independent contractors, CROs, CMOs, vendors or principal investigators, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, curtailment of our operations, disclosure of our confidential information and imprisonment, any of which could adversely affect our ability to operate our business and our results of operations.

If any of our service providers are later legally deemed to be employees, we could be subject to employment and tax withholding liabilities and other additional costs as well as other multiple damages and attorneys' fees.

We rely on independent third parties to provide certain services to us. We structure our relationships with these outside service providers in a manner that we believe results in an independent contractor relationship, not an employee relationship. An independent contractor is generally distinguished from an employee by his or her degree of autonomy and independence in providing services. A high degree of autonomy and independence is generally indicative of an independent contractor relationship, while a high degree of control is generally indicative of an employment relationship. Tax or other regulatory authorities may challenge our characterization of services providers as independent contractors both under existing laws and regulations and under laws and regulations adopted in the future. If such regulatory authorities or state, federal or foreign courts were to determine that our service providers are employees and not independent contractors, we would, among other things, be required to withhold income taxes, to withhold and pay Social Security, Medicare and similar taxes, to pay unemployment and other related payroll taxes, and to provide certain employee benefits. We could also be liable for unpaid past taxes, interest and other costs and subject to penalties. Likewise, our service providers themselves may later challenge their classification as independent contractors, which may result in additional damages, including back wages, penalties, interest and attorneys' fees. As a result, any legally binding determination that the service providers we characterize as independent contractors are actually our employees could have a material adverse effect on our business, financial condition and results of operations.

The long-term effects of the Merger with Keryx may result in a material adverse effect on our business and financial position.

We completed the Merger on December 12, 2018, but have faced and may continue to face, adverse effects, some of which may be material, including, but not limited to (i) diversion of the attention of management and key personnel and potential disruption of our ongoing business, (ii) challenges of managing a larger company, including challenges of conforming

standards, controls, procedures and accounting and other policies and compensation structures, (iii) difficulties in achieving anticipated cost savings, (iv) declines in our results of operations, financial condition or cash flows, and (v) potential liabilities, adverse consequences, increased expenses or other problems associated with our company following completion of the Merger. Many of these factors are outside of our control, and any one of them could result in increased costs, decreased expected revenues and further diversion of management time and energy, which could materially impact our business, financial statements and prospects and cause a decline in the market price of our common stock.

In addition, following the Merger, we became responsible for Keryx's liabilities and obligations, including with respect to legal, financial, regulatory and compliance matters, including certain post-approval regulatory requirements with respect to Auryxia and obligations under collaboration, license, supply and manufacturing agreements. These obligations have, and will continue to, result in additional cost and investment by us and, if we have underestimated the amount of these costs and investments or if we fail to satisfy any such obligations, we may not realize the anticipated benefits of the transaction.

Further, it is possible that there may be unknown, contingent or other liabilities or problems that may arise in the future, the existence and/or magnitude of which we were previously unaware. Any such liabilities or problems could have an adverse effect on our business, financial condition or results of operations.

Lawsuits have been filed challenging the Merger and additional lawsuits may be filed in the future. Any monetary damages or other adverse judgment would have a material adverse effect on us.

There is an ongoing appeal of a putative class action lawsuit filed in federal court, and ongoing putative class action lawsuits in state court, each filed by purported Keryx shareholders challenging the disclosures made in connection with the Merger. See Part I, Item 3. Legal Proceedings for further information relating to the lawsuits. Additional lawsuits arising out of the Merger may be filed in the future. We have expended and may continue to be required to expend significant resources in the defense of these lawsuits, including but not limited to, costs associated with the indemnification of Keryx and Akebia directors and officers, and the lawsuits, regardless of outcome, could have a negative effect on our reputation, stock price and results of operations. In addition, monetary damages or any other adverse judgment would have a material adverse effect on our business and financial position.

Our financial statements include goodwill and an intangible asset as a result of the Merger. The intangible asset has become impaired and could become further impaired in the future under certain conditions. In addition, goodwill could become impaired in the future under certain conditions. Any potential future impairment of goodwill or intangible assets may significantly impact our results of operations and financial condition.

As of December 31, 2021, we had approximately $163.2 million of goodwill and a definite lived intangible asset from the Merger. In accordance with generally accepted accounting principles, or GAAP, we are required annually, or more frequently upon certain indicators of impairment, to review our estimates and assumptions underlying the fair value of our goodwill and our definite lived intangible assets when indicators of impairment are present. Events giving rise to impairment of goodwill or intangible assets are an inherent risk in the pharmaceutical industry and often cannot be predicted.

Conditions that could indicate impairment and necessitate such a review include, but are not limited to, Auryxia's commercial performance, our inability to execute on our strategic initiatives, the deterioration of our market capitalization such that it is significantly below our net book value, a significant adverse change in legal factors, unexpected adverse business conditions, and an adverse action or assessment by a regulator. To the extent we conclude that goodwill and/or definite lived intangible assets have become impaired, we may be required to incur material write-offs relating to such impairment and any such write-offs could have a material impact on our future operating results and financial position. For example, in the second quarter of 2020, in connection with a routine business review, we reduced our short-term and long-term Auryxia revenue forecast. This reduction was primarily driven by the impact of the September 2018 CMS decision that Auryxia would no longer be covered by Medicare for the treatment of the IDA Indication. While this decision does not impact CMS coverage for the use of Auryxia for the control of serum phosphorus levels in adult patients with CKD on dialysis, or the Hyperphosphatemia Indication, it requires all Auryxia prescriptions for Medicare patients to undergo a prior authorization to ensure their use of Auryxia for the Hyperphosphatemia Indication. As a result, we recorded an impairment charge of $115.5 million during the three months ended June 30, 2020, which was entirely allocated to our only intangible asset, the developed product rights for Auryxia, and made a corresponding adjustment to the estimated useful life of the developed product rights for Auryxia, which we again adjusted during the three months ended December 31, 2020. The estimates, judgments and assumptions used in our impairment testing, and the results of our testing, are discussed in Note 9 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K. If these estimates, judgments and assumptions change in the future, including if the Auryxia asset group does not meet its current forecasted projections, additional impairment charges related to goodwill or our intangible asset could be recorded in the future and additional corresponding adjustments may need to be made to the estimated useful life of the developed product rights for Auryxia, which could materially impact our financial position, certain of our material agreements, and our future operating results.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of Auryxia or vadadustat, if approved.

We face an inherent risk of product liability as a result of the clinical and commercial use of Auryxia and vadadustat. For example, we may be sued if Auryxia or vadadustat allegedly causes injury or is found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product or product candidate, negligence, strict liability and breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of Auryxia or vadadustat, if approved. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased demand for Auryxia or vadadustat, if approved;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- delay or termination of clinical trials;
- our inability to continue to develop Auryxia or vadadustat;
- significant costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to study subjects or patients;
- product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- decreased demand for Auryxia or vadadustat, if approved;
- loss of revenue;
- the inability to commercialize Auryxia or vadadustat, if approved; and
- a decline in our stock price.

Failure to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance that we believe is appropriate for our company. Although we maintain product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have insufficient or no coverage. If we have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, we may not have, or be able to obtain, sufficient capital to pay such amounts. In addition, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost. We also may not be able to obtain additional insurance coverage that will be adequate to cover additional product liability risks that may arise. Consequently, a product liability claim may result in losses that could be material to our business.

We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we operate in a demanding regulatory environment, and we have and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and certain corporate governance practices. In particular, our compliance with Section 404 of the Sarbanes-Oxley Act has required and will continue to require that we incur substantial accounting-related expenses and expend significant management efforts. Our testing, or the testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner. If we are not able to comply with the requirements of the Sarbanes-Oxley Act, we could be subject to sanctions or investigations by the SEC, the Nasdaq Global Market or other regulatory authorities, which would require additional financial and management resources and could adversely affect the market price of our securities. Furthermore, if we cannot provide reliable financial reports or prevent fraud, including as a result of remote working by our employees in connection with COVID-19, our business and results of operations would likely be materially and adversely affected.

We cannot predict or estimate the amount of additional costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by

regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our Ninth Amended and Restated Certificate of Incorporation, as amended, or Charter, and our Amended and Restated By-Laws, or Bylaws, as amended to date, contain provisions that eliminate, to the maximum extent permitted by the General Corporation Law of the State of Delaware, or DGCL, the personal liability of our directors and executive officers for monetary damages for breach of their fiduciary duties as a director or officer. Our Charter and our Bylaws also provide that we will indemnify our directors and executive officers and may indemnify our employees and other agents to the fullest extent permitted by the DGCL.

In addition, as permitted by Section 145 of the DGCL our Bylaws and our indemnification agreements that we have entered into with our directors and executive officers provide that:

- We will indemnify our directors and officers, as defined in our Bylaws, for serving us in those capacities or for serving other related business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of Akebia and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- The rights conferred in our Bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

Any claims for indemnification made by our directors or officers could impact our cash resources and our ability to fund the business.

Our ability to use net operating losses to offset future taxable income may be subject to certain limitations.

Under Section 382 of the Internal Revenue Code, or Section 382, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. On December 12, 2018, we completed the Merger, which we believe has resulted in an ownership change under Section 382. In addition, the Tax Cuts and Jobs Act, including amendments made by the CARES Act, includes changes to United States federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to fully offset taxable income in the future. Future changes in our stock ownership, many of which are outside of our control, could result in an additional ownership change under Section 382. As a result, if we generate taxable income, our ability to use our pre-change NOL carryforwards to offset federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. At the state level, state net operating losses generated in one state cannot be used to offset income generated in another state and there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating United States taxable income. As described above under "—Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the United States taxable income necessary to utilize our NOLs.

Our Charter designates the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our Charter provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a

claim against us arising pursuant to any provision of the DGCL our Charter or our Bylaws, or (iv) any other action asserting a claim against us, our directors, officers or other employees that is governed by the internal affairs doctrine. Under our Charter, this exclusive forum provision will not apply to claims that are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Exchange Act, or the rules and regulations thereunder. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our Charter described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our Charter inapplicable to, or unenforceable with respect to, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

We are currently subject to legal proceedings that could result in substantial costs and divert management's attention, and we could be subject to additional legal proceedings.

We are currently subject to legal proceedings as described in Part I, Item 3. Legal Proceedings and additional claims may arise in the future. In addition, securities class action and derivative lawsuits and other legal proceedings are often brought against companies for any of the risks described in this Annual Report on Form 10-K following a decline in the market price of their securities. In connection with any litigation or other legal proceedings, we could incur substantial costs, and such costs and any related settlements or judgments may not be covered by insurance. In addition, if other resolution or actions taken as a result of legal proceedings were to restrain our ability to operate or market our products and services, our consolidated financial position, results of operations or cash flows could be materially adversely affected. We could also suffer an adverse impact on our reputation, negative publicity and a diversion of management's attention and resources, which could have a material adverse effect on our business.

Risks Related to our Common Stock

Our stock price has been and may continue to be volatile, which could result in substantial losses for holders or future purchasers of our common stock and lawsuits against us and our officers and directors.

Our stock price has been and will likely continue to be volatile. The stock market in general and the market for similarly situated biopharmaceutical companies specifically have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. Since our initial public offering in March 2014, the price of our common stock as reported on The Nasdaq Global Market has ranged from a low of $1.71 on February 14, 2022 to a high of $31.00 on June 20, 2014. The daily closing market price for our common stock has varied between a high price of $5.06 on February 8, 2021 and a low price of $2.26 on December 31, 2021 in the twelve-month period ending on December 31, 2021. During this time, the price of our common stock has ranged from an intra-day low of $2.20 per share to an intra-day high of $5.14 per share. The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, including, among others, developments related to and results of our research or clinical trials, developments related to our regulatory submissions and commercialization of Auryxia, vadadustat, if approved, and any other product candidates, announcements by us or our competitors of significant transactions or strategic collaborations, negative publicity around Auryxia or vadadustat, regulatory or legal developments in the United States and other countries, developments or disputes concerning our intellectual property, the recruitment or departure of key personnel, actual or anticipated changes in estimates as to financial results, changes in the structure of healthcare payment systems, market conditions in the biopharmaceutical sector and other factors beyond our control. As a result of this volatility, our shareholders may not be able to sell their common stock at or above the price at which they purchased it.

In addition, companies that have experienced volatility in the market price of their stock have frequently been the subject of securities class action and shareholder derivative litigation. See Part I, Item 3. Legal Proceedings for information concerning securities class action and shareholder derivative lawsuits initiated against Keryx and certain current and former directors and officers of ours and Keryx's. In addition, we could be the target of other such litigation in the future. Class action and shareholder derivative lawsuits, whether successful or not, could result in substantial costs, damage or settlement awards and a diversion of our management's resources and attention from running our business, which could materially harm our reputation, financial condition and results of operations.

The issuance of additional shares of our common stock or the sale of shares of our common stock by any of our directors, officers or significant shareholders will dilute our shareholders' ownership interest in Akebia and may cause the market price of our common stock to decline.

Most of our outstanding common stock can be traded without restriction at any time. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock.

As of December 31, 2021 and based on the amounts reported in the most recent filings made under Section 13(d) and 13(g) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, BlackRock, Inc., or BlackRock, beneficially owned approximately 8.0% of our outstanding shares of common stock, the Vanguard Group, or Vanguard, beneficially owned approximately 7.5% of our outstanding shares of common stock, and State Street Corporation, or State Street, beneficially owned approximately 6.6% of our outstanding shares of common stock. By selling a large number of shares of common stock, BlackRock, Vanguard, or State Street could cause the price of our common stock to decline. In addition, we previously entered into a Fourth Amended and Restated Investors' Rights Agreement, as amended, or the IRA, with our former director, Muneer Satter, who as of December 31, 2021 held less than 3% of our outstanding shares of common stock. Pursuant to the IRA, Mr. Satter has the right, subject to certain conditions and with certain exceptions, to require us to file registration statements covering the shares common stock he owns, or to include his shares in registration statements that we may file or in public offerings of our shares of common stock. Following their registration and sale under the applicable registration statement, those shares would become freely tradable.

In addition, in connection with the Vifor Second Amended Agreement, in February 2022, we entered into an investment agreement with Vifor Pharma, or the Investment Agreement, pursuant to which we sold an aggregate of 4,000,000 shares of our common stock to Vifor Pharma, representing 2.2% our outstanding common stock. Vifor Pharma beneficially owns an aggregate of 4.2% of our outstanding common stock. These shares have not been registered pursuant to the Securities Act of 1933, or the Act, and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Act and Rule 506 promulgated thereunder, but if they are registered in the future, those shares would become freely tradable and, if a large portion of such shares are sold, could cause the price of our common stock to decline.

We have a significant number of shares that are subject to outstanding options, restricted stock units and a warrant, and in the future we may issue additional options, restricted stock units, warrants or other derivative securities convertible into our common stock. The exercise or vesting of any such options, restricted stock units, warrants or other derivative securities, and the subsequent sale of the underlying common stock, could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. Also, the Merger was financed by the issuance of shares of our common stock to shareholders of Keryx, comprising approximately 50.6% of our issued and outstanding shares of common stock, calculated based on our fully diluted market capitalization as of the date of signing the Agreement and Plan of Merger relating to the Merger. Keryx shareholders may decide not to hold the shares of our common stock they received in the Merger. Other Keryx shareholders, such as funds with limitations on the amount of stock they are permitted to hold in individual issuers, may be required to sell the shares of our common stock they received in the Merger. Such sales of our common stock could result in higher than average trading volume and may cause the market price for our common stock to decline.

In addition, we currently have on file with the SEC a shelf registration statement, which allows us to offer and sell up to $300 million in registered securities, such as common stock, preferred stock, debt securities, warrants and units, from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale, including a a sales agreement prospectus that covers the offering, issuance and sale by us of up to a maximum aggregate offering price of up to $25,268,163 of our common stock that may be issued and sold from time to time under an amended and restated sales agreement with Cantor Fitzgerald & Co.

Sales of substantial amounts of shares of our common stock or other securities by our employees or our other shareholders or by us under our shelf registration statement, pursuant to at-the-market offerings or otherwise, could dilute our stockholders, lower the market price of our common stock and impair our ability to raise capital through the sale of equity securities.

Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval.

As of December 31, 2021, our executive officers, directors and principal stockholders, in the aggregate, beneficially owned shares representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

Provisions in our organizational documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our Charter and our Bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our Board of Directors is responsible for appointing certain members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board of Directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our Board of Directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified Board of Directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our Board of Directors pursuant to a resolution adopted by a majority of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our Board of Directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our Board of Directors may be filled only by a majority of directors then in office, even though less than a quorum;
- require a supermajority vote of 75% of the holders of our capital stock entitled to vote or the majority vote of our Board of Directors to amend our Bylaws; and
- require a supermajority vote of 85% of the holders of our capital stock entitled to vote to amend the classification of our Board of Directors and to amend certain other provisions of our Charter.

These provisions, alone or together, could delay or prevent hostile takeovers, changes in control or changes in our management.
In addition, Section 203 of the DGCL prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Because we do not anticipate paying any cash dividends on our capital in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our capital stock and we currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. Any payment of cash dividends in the future would be at the discretion of our Board of Directors and would depend on, among other things, our earnings, financial condition, capital requirements, level of indebtedness, statutory and contractual restrictions applying to the payment of dividends and other considerations that the Board of Directors deems relevant. In addition, the terms of the Loan Agreement preclude us from paying cash dividends and future debt agreements may preclude us from paying cash dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters are located in Cambridge, Massachusetts. We currently lease approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts, and 27,300 square feet of office space in Boston, Massachusetts. Excluding renewal options, the lease for our Cambridge, Massachusetts office space expires on September 11, 2026 and the lease for the Cambridge, Massachusetts lab space expires on January 31, 2025. In February 2022 we extended the term of the lease for our Boston, Massachusetts office space, such that the lease expires on July 31, 2031. In September 2019, we entered into an agreement to sublease the Boston office space to Foundation Medicine, Inc., which will expire on February 28, 2023. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms for our future growth.

Item 3. Legal Proceedings

Legal Proceedings Relating to Vadadustat

Opposition Proceedings Against Akebia

In July 2011, a third party filed an opposition to our issued European Patent No. 2044005, or the ’005 EP Patent, in the European Patent Office, or the EPO. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the EPO maintained the ’005 EP Patent. This decision resulted in the maintenance of a claim directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases, including, but not limited to, anemia. Both parties appealed the decision of the Opposition Division of the EPO. On February 27, 2018, we withdrew the ’005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia.

In September 2018, Dr. Reddy’s Laboratories Limited filed an opposition to our issued Indian Patent No. 287720 in the Indian Patent Office.

Proceedings Filed by Akebia Against FibroGen, Inc.

Europe

We filed an opposition in the EPO against FibroGen, Inc.’s, or FibroGen’s, European Patent No. 1463823, or the ’823 EP Patent on December 5, 2013, and an oral proceeding took place March 8 and 9, 2016. Following the oral proceeding, the Opposition Division of EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision.

On May 13, 2015, May 20, 2015 and July 6, 2015, we filed oppositions to FibroGen’s European Patent Nos. 2322155, or the ’155 EP Patent, 1633333, or the ’333 EP Patent, and 2322153, or the ’153 EP Patent in the EPO, respectively, requesting the patents be revoked in their entirety. These method of use patents do not prevent persons from using the compound for other uses, including any previously known use of the compound. In particular, these patents do not claim methods of using any of our product candidates for purposes of inhibiting HIF-PH for the treatment of anemia due to chronic kidney disease, or CKD. While we do not believe these patents will prevent us from commercializing vadadustat for the treatment of anemia due to CKD, we filed these oppositions to provide us and our collaborators with maximum flexibility for developing vadadustat and our pipeline of investigational oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor compounds.

Oppositions to the ’155 EP Patent and the ’153 EP Patent were also filed in the EPO by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH, or, collectively, Bayer. Glaxo withdrew its oppositions on March 2, 2020 and Bayer withdrew its oppositions on June 30, 2021.

With regard to the opposition that we filed in Europe against the ’333 EP Patent, an oral proceeding took place on December 8 and 9, 2016. Following the oral proceeding, the Opposition Division of the EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. On December 9, 2016, FibroGen filed a notice to appeal the decision to revoke the ’333 EP Patent. The Board of Appeal held an oral proceeding on this appeal on February 24 and 25, 2022, during which proceeding the '333 EP Patent was maintained in restricted form. The ‘333 EP patent was originally granted with four independent claims, one of which was found obvious on appeal. The remaining claims are directed to: treatment of anemia of chronic disease in subjects having a percent transferrin

saturation of less than 20% (claim 1), treatment of anemia that is refractory to treatment with exogenously administered erythropoietin (claim 6), and treatment of iron deficiency (claim 15).

In oral proceedings held on May 29, 2017, regarding the ’155 EP Patent, the European Opposition Division ruled that the ’155 EP Patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen filed a notice to appeal the decision to revoke the ’155 EP Patent on May 29, 2017. An oral proceeding for the appeal was held on February 22, 2022, during which proceeding the Board of Appeal maintained the revocation of the ‘155 EP Patent in its entirety.

Subsequently, in related oral proceedings held on May 31, 2017 and June 1, 2017 for the ’153 EP Patent, the Opposition Division of the EPO maintained the patent after FibroGen significantly narrowed the claims to an indication for which vadadustat is not intended to be developed. We and Glaxo separately filed notices to appeal the decision to maintain the ’153 EP Patent on November 9, 2017. Bayer filed a notice to appeal the decision on November 14, 2017. Glaxo withdrew its appeal on March 2, 2020 and Bayer withdrew its appeal on June 30, 2021. An oral proceeding for the appeal was held on February 21, 2022, during which proceeding the Board of Appeal revoked the ‘153 patent in its entirety.

On April 3, 2019, we filed oppositions to FibroGen’s European Patent Nos. 2289531, or the ’531 EP Patent, and 2298301, or the ’301 EP Patent in the EPO, respectively, requesting the patents be revoked in their entirety. Oral proceedings for oppositions to the two patents were held on September 7-8 and 10, 2021. Following oral proceedings, the Opposition Division of the EPO maintained certain claims in amended form in the two patents. We do not expect the Opposition Division’s decision on the two patents to have any effect on our commercialization of vadadustat in Europe.

On February 10, 2020, we filed an opposition to FibroGen’s European Patent No. 2324834, or the ’834 EP Patent, in the EPO requesting the patent to be revoked in its entirety. On October 19, 2021, FibroGen submitted a request to the Opposition Division to terminate these opposition proceedings and revoke the '834 patent.

Canada

On May 21, 2018, we filed a Statement of Claim in Canadian Federal Court to challenge the validity of three of FibroGen’s HIF-related patents in Canada: CA 2467689, CA 2468083, and CA 2526496. On June 25, 2020, the parties agreed to dismiss the CA 2467689 patent from the lawsuit. On February 16, 2021, the parties agreed to dismiss the lawsuit in its entirety.

Japan

On June 2, 2014, we filed an invalidity proceeding before the Japan Patent Office, or JPO, against certain claims of FibroGen’s Japanese Patent No. 4804131, or the ’131 JP Patent, which is the Japanese counterpart to the ’823 EP Patent, and the JPO issued a preliminary decision finding all of the challenged claims to be invalid. FibroGen subsequently amended the claims and the JPO accepted the amendments. The resulting ‘131 JP Patent does not cover vadadustat or any pyridine carboxamide compounds.

On June 22, 2018, we and our collaboration partner in Japan, Mitsubishi Tanabe Pharma Corporation, or MTPC, jointly filed a Request for Trial before the JPO to challenge the validity of one of FibroGen’s HIF-related patents in Japan, JP4845728. On July 20, 2018 and August 13, 2018, we and MTPC jointly filed a Request for Trial before the JPO to challenge the validity of two additional FibroGen HIF-related patents in Japan, JP5474872 and JP5474741, respectively. On September 26, 2019, the JPO conducted an invalidation trial for JP5474872 and JP4845728. On November 11, 2019, the JPO conducted an invalidation trial for JP5474741. On February 10, 2020, the JPO issued a pre-notice of a trial decision for JP4845728, which invalidated all claims except two claims in amended form. On March 11, 2020, the JPO issued a pre-notice of a trial decision for JP5474872, which invalidated all claims except one claim in amended form. On April 2, 2020, the JPO issued a pre-notice of a trial decision for JP5474741, which invalidated all claims except two claims in amended form. We expect the JPO to issue a final decision this year. We do not believe these decisions will prevent our collaboration partner MTPC from commercializing vadadustat for the treatment of anemia due to CKD in Japan.

United Kingdom

On December 13, 2018, we and our collaboration partner, Otsuka Pharmaceutical Co. Ltd., or Otsuka, filed Particulars of Claim in the Patents Court of the United Kingdom to challenge the validity of FibroGen’s six HIF-related patents in the UK: the ’823 EP Patent (UK), the ’333 EP Patent (UK), the ’153 EP Patent (UK), the ’155 EP Patent (UK), European Patent (UK) No. 2,289,531, or the ’531 EP Patent (UK), and European Patent (UK) No. 2,298,301, or the ’301 EP Patent (UK). In May 2019, Astellas Pharma Inc., or Astellas, the exclusive licensee of FibroGen’s HIF-related patents, sued Akebia and Otsuka for patent infringement in the Patents Court of the UK. In September 2019, we and Otsuka filed an Amended Particulars of Claim to

include FibroGen's European Patent No. 1487472, or the '472 EP Patent (UK). On February 28, 2020, the parties agreed to dismiss the '472 EP Patent (UK) from the trial.

A trial was conducted in March 2020. On April 20, 2020, the Patents Court of the UK issued a judgment in favor of Akebia, which invalidated all the claims at issue in each of the '823 EP Patent (UK), the '333 EP Patent (UK), the '153 EP Patent (UK), the '155 EP Patent (UK) and the '301 EP Patent (UK). The '531 EP Patent (UK) was amended to a single claim to recite one specific compound; this claim was held to be valid but not infringed by vadadustat. On June 11, 2020, FibroGen and Astellas appealed the Patents Court's judgment on the invalidity of the '823 EP Patent (UK), the '301 EP Patent (UK), the '333 EP Patent (UK), the '153 EP Patent (UK), and the '155 EP Patent (UK) in the Court of Appeal (Civil Division). On June 8, 2021 - June 10, 2021, the United Kingdom Court of Appeal held a three-day hearing for the appeal. On August 24, 2021, the Court of Appeal issued a judgment, which reversed the Patents Court's judgment on the invalidity of the '823 EP Patent (UK) and maintained certain claims of the '823 EP Patent (UK) and the '301 EP Patent (UK) in amended form, and which affirmed the Patents Court's judgment on the invalidity of the '333 EP Patent (UK), the '155 EP Patent (UK), and the '153 EP Patent (UK). Akebia and Otsuka are seeking permission to appeal to the UK Supreme Court. We do not expect the UK Court of Appeal's judgment to have any effect on our commercialization of vadadustat in the UK.

United States

On March 29, 2021, we and our collaboration partner Otsuka America Pharmaceutical, Inc. filed a lawsuit against FibroGen and AstraZeneca AB in the United States District Court for the District of Delaware to seek a declaratory judgment of non-infringement and invalidity of FibroGen's twelve HIF-related patents in the United States: U.S. Patent Nos. 8,318,703, 8,466,172, 8,614,204, 9,920,011, 8,629,131, 8,604,012, 8,609,646, 8,604,013, 10,626,090, 10,894,774, 10,882,827, and 10,927,081. The defendants filed a motion to dismiss the lawsuit on June 4, 2021. We and Otsuka filed an opposition to the defendants' motion on July 2, 2021, and the defendants filed a reply brief on July 16, 2021. We are awaiting the Court's decision on the Defendant's motion to dismiss.

Legal Proceedings Relating to Auryxia

ANDA Litigation

On October 31, 2018, November 6, 2018, December 24, 2018 and February 4, 2019, Keryx Biopharmaceuticals, Inc., or Keryx, received Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the U.S. Food and Drug Administration, or FDA, by Lupin Atlantis Holdings SA, or Lupin, Teva Pharmaceuticals USA, Inc., or Teva, Chemo Research S.L., or Chemo, and Mylan Pharmaceuticals Inc., or Mylan, respectively, requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). On December 13, 2018, Keryx and its licensors, Panion & BF Biotech, Inc., or Panion, and Chen Hsing Hsu, M.D., filed a complaint for patent infringement against Lupin and Lupin Ltd., or the Lupin Defendants, in the United States District Court for the District of Delaware, or the Delaware District Court, arising from Lupin's ANDA filing with the FDA. On December 19, 2018, Keryx and Panion filed a complaint for patent infringement against Teva and Teva Pharmaceutical Industries Limited, or the Teva Defendants, in the Delaware District Court arising from Teva's ANDA filing with the FDA. On February 1, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Chemo and Insud Pharma S.A., or the Chemo Defendants, in the Delaware District Court arising from Chemo's ANDA filing with the FDA. On March 15, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Mylan in the United States District Court for the Northern District of West Virginia arising from Mylan's ANDA filing with the FDA. On April 18, 2019, Keryx, Panion and Dr. Hsu filed a motion with the Judicial Panel on Multidistrict Litigation seeking to consolidate these four cases in the Delaware District Court for pretrial proceedings.

On March 29, 2019, April 2, 2019, and April 12, 2019, Keryx received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA by Lupin Ltd., Watson Laboratories, Inc., or Watson, a wholly-owned, indirect subsidiary of Teva, and Par Pharmaceutical, Inc., or Par, an Endo International company, or Endo, respectively, requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). On May 10, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Lupin Ltd. in the Delaware District Court arising from Lupin Ltd.'s ANDA filing with the FDA. On May 10, 2019, Keryx and Panion filed a complaint for patent infringement against Watson and the Teva Defendants, or the Watson Defendants, in the Delaware District Court arising from Watson's ANDA filing with the FDA. On May 15, 2019, Keryx and Panion filed a complaint for patent infringement against the Watson Defendants in the United States District Court for the District of Nevada, or the Nevada District Court, from Watson's ANDA filing with the FDA. On May 23, 2019, Keryx and Panion filed a complaint for patent infringement against Par in the Delaware District Court arising from Par's ANDA filing with the FDA. On May 24, 2019, Keryx and Panion filed a complaint for patent infringement against Par, in the United States District Court for the Southern District of New York, or the Southern New York District Court, arising from Par's ANDA filing with the FDA. On June 4, 2019, Keryx and Panion filed a notice of voluntary dismissal to dismiss the suit in the Nevada District Court in view of the Watson Defendants' consent to venue of the Delaware District Court. On June 26, 2019,

Keryx, Panion and Dr. Hsu notified the Judicial Panel on Multidistrict Litigation of additional actions in the Delaware District Court against the Lupin Defendants and the Watson Defendants. On July 31, 2019, the Judicial Panel on Multidistrict Litigation issued an order to consolidate all of our ANDA cases in Delaware District Court for pretrial proceedings. On August 26, 2019, Keryx filed an amended complaint against the Lupin Defendants in the Delaware District Court arising from the Lupin Defendants' ANDA filings with the FDA. On September 19, 2019, the Delaware District Court set a trial date for February 8, 2021. The trial was rescheduled for June 28, 2021. On January 13, 2021, the Delaware District Court vacated the deadlines for the case involving Mylan pending resolution of a discovery dispute.

On July 22, 2019, Keryx received from Teva a supplemental Paragraph IV certification notice letter regarding its ANDA. On July 22, 2019, Keryx received from Watson a supplemental Paragraph IV certification notice letter regarding its ANDA. On July 31, 2019, Keryx received from Lupin a supplemental Paragraph IV certification notice letter regarding its ANDA. On July 31, 2019, Keryx received from Lupin Ltd. a supplemental Paragraph IV certification notice letter regarding its ANDA. On September 17, 2019, Keryx received from Par a supplemental Paragraph IV certification notice letter regarding its ANDA. On October 16, 2019, Keryx received from Mylan a supplemental Paragraph IV certification notice letter regarding its ANDA. On May 14, 2020, Keryx received from Chemo a supplemental Paragraph IV certification notice letter regarding its ANDA.

On April 27, 2020, the Delaware District Court conducted a Markman hearing concerning certain claim construction issues with respect to four Orange Book-listed patents, and issued an order in favor of Keryx.

On August 2, 2019, Keryx and Panion entered into a settlement and license agreement with Par. This settlement resolved patent litigation brought by Keryx and Panion in response to Par's ANDA seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion granted Par a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation between Keryx and Panion and Par regarding Auryxia patents pending in the Delaware District Court and the Southern New York District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On August 5, 2019, the parties filed a request to stay the litigation pending a review of the settlement and license agreement by these regulatory authorities. On September 6, 2019 and September 9, 2019, the Southern New York District Court and the Delaware District Court, respectively, entered a stipulation and order of dismissal filed by the parties to terminate the actions against Par.

On April 30, 2020, Keryx and Panion entered into a settlement and license agreement with Teva and Watson. This settlement resolved patent litigation brought by Keryx and Panion in response to Teva and Watson's ANDAs seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion granted Teva and Watson a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation between Keryx and Panion and Watson and Teva regarding Auryxia patents pending in the Delaware District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On May 4, 2020, the Delaware District Court entered a stipulation and order of dismissal filed by the parties to terminate the action against Teva and Watson.

On September 24, 2020, Keryx, Panion and Dr. Hsu entered into a settlement and license agreement with the Lupin Defendants. This settlement resolved patent litigation brought by Keryx and Panion in response to Lupin and Lupin Ltd.'s ANDAs seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion granted Lupin and Lupin Ltd. a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation among Keryx, Panion, the Lupin Defendants and Dr. Hsu regarding Auryxia patents pending in the Delaware District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On October 5, 2020, the Delaware District Court entered a stipulation and order of dismissal filed by the parties to terminate the action against the Lupin Defendants.

On March 25, 2021, Keryx and Panion entered into a settlement and license agreement with the Chemo Defendants. This settlement resolved patent litigation brought by Keryx and Panion in response to Chemo's ANDA seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion granted Chemo a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation among Keryx, Panion, and the Chemo Defendants regarding Auryxia patents pending in the Delaware District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On March 26,

2021, the Delaware District Court entered a stipulation and order of dismissal filed by the parties to terminate the action against the Chemo Defendants.

On September 22, 2021, Keryx, Panion and Dr. Hsu entered into a settlement and license agreement with Mylan. This settlement resolved patent litigation brought by Keryx, Panion, and Dr. Hsu in response to Mylan's ANDA seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx, Panion, and Dr. Hsu granted Mylan a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation among Keryx, Panion, Dr. Hsu, and Mylan regarding Auryxia patents pending in the Delaware District Court and the North District Court of West Virginia. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On September 28, 2021, the Delaware District Court entered a stipulation and order of dismissal filed by the parties to terminate the action against Mylan.

Keryx, Panion and, as applicable, Dr. Hsu have now entered into settlement and license agreements resolving all patent litigation proceedings brought by Keryx, Panion and, as applicable, Dr. Hsu, in response to ANDAs filed by third parties seeking approval to market generic versions of Auryxia® (ferric citrate) tablets prior to the expiration of the applicable patents.

CMS Litigation

On October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts, or the Massachusetts District Court, against Centers for Medicare & Medicaid Services, or CMS, the U.S. Department of Health and Human Services, Alex M. Azar II in his official capacity as Secretary of Health and Human Services, and Seema Verma in her official capacity as administrator for CMS challenging CMS's decision that Auryxia would no longer be covered by Medicare for the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or the IDA Indication, and imposing a prior authorization requirement for Auryxia in the treatment of adult patients with CKD on dialysis, or the Hyperphosphatemia Indication. On October 29, 2019, we filed a motion for a preliminary injunction asking the Massachusetts District Court to provide relief while the lawsuit was pending, specifically, to restore coverage of Auryxia for the IDA Indication, and to remove the prior authorization requirement for Auryxia for the Hyperphosphatemia Indication. In the alternative, we filed a motion for summary judgment with the Massachusetts District Court asking it to decide the case on the merits. On February 4, 2020, the Massachusetts District Court denied our request for a preliminary injunction. We filed an expedited appeal with the Court of Appeals for the First Circuit challenging the Massachusetts District Court's denial of our motion for a preliminary injunction. The First Circuit Court of Appeals held oral argument on August 14, 2020, and affirmed the Massachusetts District Court's denial of our request for a preliminary injunction on September 30, 2020. We then attempted to reach a settlement with CMS, but we were unsuccessful in these efforts. On October 22, 2021, the parties agreed to dismiss the litigation. As a result, Auryxia remains not covered by Medicare for the IDA Indication and the prior authorization requirement for Auryxia for the Hyperphosphatemia Indication also remains in place.

Shareholder Litigation Relating to Auryxia Supply

Four putative class action lawsuits were filed against Keryx and certain of its former officers (Gregory P. Madison, Scott A. Holmes, Ron Bentsur, and James Oliviero) and consolidated in the Massachusetts District Court, captioned Karth v. Keryx Biopharmaceuticals, Inc., et al. (filed October 26, 2016, with an amended complaint filed on February 27, 2017). Plaintiff sought to represent all stockholders who purchased shares of Keryx common stock between May 8, 2013 and August 1, 2016. The complaint alleges that Keryx and the named individual defendants violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning Keryx, its supplier relationships, and future prospects, and that the allegedly misleading statements were not made known to the market until Keryx's August 1, 2016 announcement of an interruption in its supply of Auryxia.

On September 23, 2019, the Massachusetts District Court issued a Memorandum and Order denying plaintiff's motion for class certification, granting defendants' motion for judgment on the pleadings, and denying plaintiff's motion for leave to further amend his Complaint. That same day, the Massachusetts District Court entered a final judgment in favor of defendants on all claims. On September 24, 2019, plaintiff filed a notice of appeal. On June 21, 2021, the First Circuit affirmed the District Court's judgment in its entirety. The time for plaintiff to seek further appellate review has now lapsed, so the judgment in favor of Akebia and the other defendants is now final.

Two stockholder derivative complaints also were filed on December 16, 2016 against Keryx and certain of its former officers (Gregory P. Madison, Scott A. Holmes, Ron Bentsur and James Oliviero) certain of its former directors (Kevin J. Cameron, Daniel P. Regan, Steven C. Gilman, Michael Rogers Michael P. Tarnok, Joseph Feczko, Jack Kaye Wyche Fowler, Jr. and John P. Butler), some of whom are current directors and officers of ours, in the Superior Court of Massachusetts, one captioned Venkat Vara Prasad Malledi v. Keryx Biopharmaceuticals, Inc., et al., and one captioned James Anderson v. Keryx

Biopharmaceuticals, Inc., et al. Each of these two complaints generally alleged breach of fiduciary duty, unjust enrichment, abuse of control, mismanagement and corporate waste. On June 27, 2017, the Superior Court of Massachusetts granted the parties' motion to consolidate and stay the derivative litigations pending the outcome of the federal securities litigation. On July 15, 2021, the plaintiffs in these actions filed a Notice of Dismissal, without prejudice, of all claims.

Shareholder Litigation Relating to the Merger

On June 28, 2018, we entered into an Agreement and Plan of Merger with Keryx and Alpha Therapeutics Merger Sub, Inc., or the Merger Sub, pursuant to which the Merger Sub would merge with and into Keryx, with Keryx becoming a wholly owned subsidiary of ours, or the Merger. On December 12, 2018, we completed the Merger. In October and November 2018, four purported shareholders of Keryx filed four separate putative class actions, or the Merger Securities Actions, against Keryx, a former officer and director of Keryx (Jodie P. Morrison), former directors of Keryx (Kevin J. Cameron, Mark J. Enyedy, Steven C. Gilman, Michael T. Heffernan, Daniel P. Regan and Michael Rogers, some of whom are current members of our Board of Directors), and, with respect to the Rosenblatt action discussed below, the Merger Sub and Akebia, challenging the disclosures made in connection with the Merger.

Three of the Merger Securities Actions were filed in the Delaware District Court: Corwin v. Keryx Biopharmaceuticals, Inc., et al. (filed October 16, 2018); Van Hulst v. Keryx Biopharmaceuticals, Inc., et al. (filed October 24, 2018); and Andreula v. Keryx Biopharmaceuticals, Inc., et al. (filed November 1, 2018). The fourth Merger Securities Action was filed in the Massachusetts District Court: Rosenblatt v. Keryx Biopharmaceuticals, Inc., et al. (filed October 23, 2018). On February 19, 2019, the plaintiff in the Rosenblatt action filed a notice of voluntary dismissal of the action without prejudice. On March 27, 2019, the plaintiff in the Van Hulst action filed a notice of voluntary dismissal of the action without prejudice.

On April 2, 2019, the Delaware District Court granted Abraham Kiswani, a member of the putative class in both the Andreula and Corwin actions, and plaintiff John Andreula's motion to consolidate the remaining two Merger Securities Actions pending in the Delaware District Court and consolidated the Corwin and Andreula cases under the caption In re Keryx Biopharmaceuticals, Inc., or the Consolidated Federal Action. The Delaware District Court also appointed Kiswani and plaintiff Andreula as lead plaintiffs for the Consolidated Federal Action. On June 3, 2019, the lead plaintiffs filed a consolidated amended complaint in the Consolidated Federal Action, or the Consolidated Complaint. The Consolidated Complaint generally alleged that the registration statement filed in connection with the Merger contained allegedly false and misleading statements or failed to disclose certain allegedly material information in violation of Section 14(a) and 20(a) of the Exchange Act and Rule 14a-9 promulgated thereunder. The alleged misstatements or omissions related to (i) certain financial projections for Keryx and Akebia and certain financial analyses performed by our advisors and (ii) any alleged negotiations that may have taken place regarding the conversion of certain convertible notes of Keryx in connection with the Merger. The Consolidated Complaint sought compensatory and/or rescissory damages, a declaration that the defendants violated Sections 14(a) and 20(a) of the Exchange Act and Rule 14a-9 thereunder, and an award of lead plaintiffs' costs, including reasonable allowance for attorneys' fees and experts' fees. The defendants in the Consolidated Federal Action moved to dismiss the Consolidated Complaint in its entirety and with prejudice on August 2, 2019. On April 15, 2020, the Delaware District Court granted the defendants' motion and dismissed the Consolidated Complaint in its entirety. On July 2, 2020, lead plaintiffs filed a second consolidated amended complaint, or the Second Consolidated Complaint. The Second Consolidated Complaint (i) asserts the same claims under the Exchange Act as the Consolidated Complaint, (ii) names the same defendants as the Consolidated Complaint, (iii) seeks the same relief as the Consolidated Complaint and (iv) as with the Consolidated Complaint, challenges as false or misleading alleged misstatements or omissions related to certain financial projections for Keryx and Akebia and certain financial analyses performed by our advisors. The defendants in the Consolidated Federal Action moved to dismiss the Second Consolidated Complaint in its entirety with prejudice on August 10, 2020. Briefing on defendants' motion to dismiss was completed on October 7, 2021, and the Third Circuit submitted the case on the briefs without oral argument on February 10, 2022. The decision is currently pending.

On July 15, 2021, a purported former Keryx stockholder filed a putative class action in the Supreme Court of the State of New York against Akebia, a current officer of Akebia (John P. Butler), a former officer of Akebia (Jason A. Amello), former directors of Akebia (Muneer A. Satter, Scott A. Canute, Michael D. Clayman, Maxine Gowen, Duane Nash, Ronald C. Renaud, Jr., and Michael S. Wyzga), a current director of Akebia (Cynthia Smith), a former director and officer of Keryx (Jodie P. Morrison), a former officer of Keryx (Scott A. Holmes) and former directors of Keryx (Michael Rogers, Kevin J. Cameron, Steven C. Gilman, Daniel P. Regan, Mark J. Enyedy, and Michael T. Heffernan, some of whom are current members of our Board of Directors). The action is captioned Loper v. Akebia Therapeutics, Inc., et al., or the *Loper* Action. The complaint in the *Loper* Action alleges that the registration statement filed in connection with the Merger contained allegedly false and misleading statements or failed to disclose certain allegedly material information in violation of Section 11, 12(a)(2), and 15 of the Securities Act of 1933, as amended. The alleged misstatements or omissions relate to the safety, approvability, and commercial viability of vadadustat. The complaint in the *Loper* Action seeks damages including interest thereon, an award of plaintiffs' and the class's costs and expenses, including counsel fees and expert fees, and rescission, disgorgement, or such other equitable or injunctive relief that the Court deems appropriate.

On August 16, 2021, another purported former Keryx stockholder filed a putative class action making substantially similar allegations and asserting the same claims as the *Loper* Action, also in the Supreme Court of the State of New York against the same defendants named in the *Loper* Action (except for Kevin J. Cameron, Scott A. Holmes, and Daniel P. Regan). The action is captioned Panicho v. Akebia Therapeutics, Inc., et al., or the *Panicho* Action.

On September 13, 2021, the parties in the *Loper* Action and *Panicho* Action entered into a joint stipulation and proposed order, which provided for the consolidation of the two actions under the caption In re Akebia Therapeutics, Inc. Securities Litigation, or the Consolidated State Action. On October 27, 2021, plaintiffs filed a consolidated complaint in the Consolidated State Action. On January 10, 2022, defendants moved to dismiss the consolidated complaint in its entirety. Briefing on defendants' motion to dismiss is scheduled to be complete by March 28, 2022.

We deny any allegations of wrongdoing and intend to continue vigorously defending against the shareholder lawsuits described in this Legal Proceedings section. There is no assurance, however, that we will be successful in the defense of these lawsuits, or any associated appeals, or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of these actions. Moreover, we are unable to predict the outcome or reasonably estimate a range of possible losses at this time. A resolution of these lawsuits in a manner adverse to us, however, could have a material effect on our financial position and results of operations in the period in which a particular lawsuit is resolved.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock is traded on The Nasdaq Global Market under the symbol "AKBA".

Holders

At February 18, 2022, there were approximately 31 holders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared or paid any cash dividends on our common stock. We currently intend to retain earnings, if any, for use in our business and do not anticipate paying cash dividends on our common stock in the foreseeable future. In addition, the terms of our loan agreement with funds managed by Pharmakon Advisors, LP preclude us from paying cash dividends and future debt agreements may preclude us from paying cash dividends. Payment of future dividends, if any, on our common stock will be at the discretion of our Board of Directors after taking into account various factors, including our financial condition, operating results, anticipated cash needs, and plans for expansion.

Issuer Purchases of Equity Securities

None.

Recent Sales of Unregistered Securities

None.

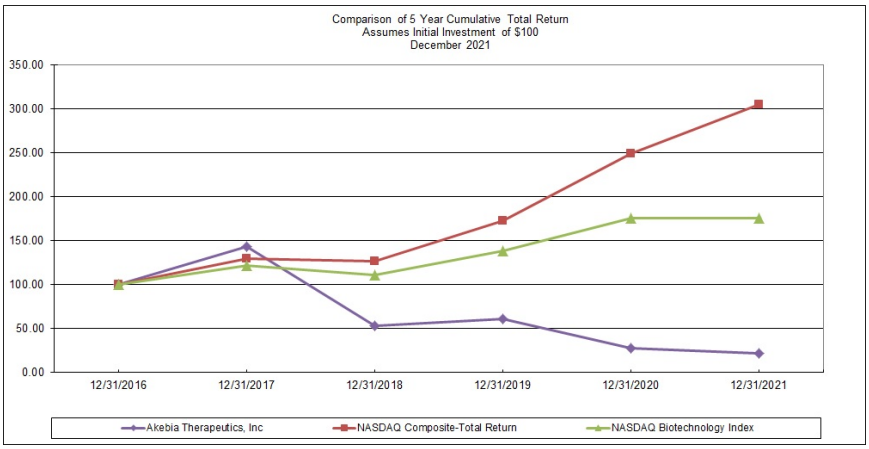
Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Comparative Stock Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or "filed" with the SEC or subject to Regulation 14A or 14C, or to the liabilities of Section 18 of the Exchange Act, except to the extent that we specifically request that this information be treated as soliciting material or we specifically incorporate it by reference into a filing under the Securities Act of 1933, as amended, or the Exchange Act.

Set forth below is a graph* comparing the total cumulative returns of Akebia Therapeutics, Inc., the Nasdaq** Composite Index and the Nasdaq Biotechnology Index. The graph assumes $100 was invested on December 31, 2016 in our common stock and each of the indices and that all dividends, if any, are reinvested. The performance shown represents past performance and should not be considered an indication of future performance.



*Prepared by Zack's Investment Research, Inc. Used with permission. All rights reserved. Copyright 1980-2022

**Index Data: Copyright NASDAQ OMX, Inc. Used with permission. All rights reserved.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12, Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters, of this Annual Report on Form 10-K.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve significant risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Please also refer to the section under the heading "Note Regarding Forward-Looking Statements."

Business Overview

We are a biopharmaceutical company with the purpose of bettering the life of each person impacted by kidney disease. Since our initial public offering in 2014, we have built a business focused on developing and commercializing innovative therapeutics that we believe serves as a foundation for future growth. We have established ourselves as a leader in the kidney community, and we remain committed to helping patients and others where we believe our current and future products have the ability to deliver value. We believe that delivering value broadly to the kidney community, as well as others who may benefit from our medicines, will result in delivering value for shareholders. Our portfolio includes a late-stage product candidate and a commercial product:

- ***Vadadustat*** is an investigational oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, or HIF, which stimulates erythropoietin, or EPO, production and leads to red blood cell, or RBC, production and improved oxygen delivery to tissues. The significance of the HIF pathway was recognized by the 2019 Nobel Prize and the

2016 Albert Lasker Basic Medical Research Award, which honored the three physician-scientists who discovered the HIF pathway and elucidated this primary oxygen sensing mechanism that is essential for survival. We believe that, based on the HIF-PH inhibitor mechanism of action and the results of our Phase 3 clinical trials, vadadustat has the potential to become the new oral standard of care for the treatment of anemia due to chronic kidney disease, or CKD.

We completed the global Phase 3 clinical development program for vadadustat in September 2020 to support regulatory filings in the United States, Europe, and other countries, which included two separate programs, INNO$_2$VATE and PRO$_2$TECT. INNO$_2$VATE evaluated vadadustat for the treatment of anemia due to CKD in adult patients on dialysis, or DD-CKD, and PRO$_2$TECT evaluated vadadustat for the treatment of anemia due to CKD in adult patients not on dialysis, or NDD-CKD.

In May of 2020, we announced positive top-line results from our Phase 3 INNO$_2$VATE program that showed vadadustat was non-inferior to darbepoetin alfa, an injectable erythropoiesis-stimulating agent, or ESA, with respect to hematological efficacy (change in hemoglobin concentration) and cardiovascular safety (assessed in a time to the first occurrence of a major adverse cardiovascular event, or MACE, analysis, which is the composite of all-cause mortality, nonfatal myocardial infarction, or a nonfatal stroke) in treating anemia due to CKD in DD-CKD adult patients. In addition to meeting the primary endpoints of the INNO$_2$VATE program, vadadustat met the key secondary hematological efficacy endpoint in each of the two studies in the program and also met the program's key secondary safety endpoints. The results of the INNO$_2$VATE program were presented at American Society of Nephrology, or ASN, in October of 2020 and published in the *New England Journal of Medicine* in April of 2021.

In September of 2020, we announced top-line results from our Phase 3 PRO$_2$TECT program that showed vadadustat was non-inferior to darbepoetin alfa with respect to hematological efficacy in treating anemia due to CKD in NDD-CKD adult patients. While the PRO$_2$TECT data showed that vadadustat achieved both the primary and key secondary hematological efficacy endpoints, it did not meet the program's primary cardiovascular safety, or MACE, endpoint. These cardiovascular outcomes contrast with those reported within the INNO$_2$VATE program, which evaluated vadadustat for the treatment of anemia due to CKD in DD-CKD adult patients. The results of the PRO$_2$TECT program were presented at ASN in October of 2020 and published in the *New England Journal of Medicine* in April of 2021.

We submitted a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, for vadadustat in March of 2021 for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. Our NDA submission was accepted for filing by the FDA in May of 2021 and the FDA has indicated that they are not currently planning to hold an Advisory Committee meeting to discuss the NDA for vadadustat. The FDA also assigned the application standard review and a Prescription Drug User Fee Act, or PDUFA, target action date of March 29, 2022. Our collaboration partner, Otsuka Pharmaceutical Co. Ltd., or Otsuka, submitted a Marketing Authorization Application, or MAA, for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients to the European Medicines Agency, or EMA, in October 2021. As vadadustat did not meet the PRO$_2$TECT program's primary safety endpoint, we are remaining cautious in our outlook for potential approval of vadadustat in NDD-CKD adult patients in the United States and Europe.

In June of 2020, we announced the first regulatory approval of vadadustat for the treatment of anemia due to CKD in DD-CKD and NDD-CKD adult patients in Japan. Our collaboration partner in Japan, Mitsubishi Tanabe Pharma Corporation, or MTPC, commenced commercial sales of vadadustat in Japan under the trade name, Vafseo™, in August 2020. In addition, MTPC filed a new drug application for vadadustat for the treatment of anemia due to CKD in adult patients in Taiwan in January of 2022.

In addition to anemia due to CKD, we believe that vadadustat has the potential to treat other serious or life-threatening conditions, including preventing and lessening the severity of acute respiratory distress syndrome, or ARDS, a complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, infection. More specifically, in July of 2020, we announced an investigator-sponsored clinical study by The University of Texas Health Science Center at Houston, or UTHealth, in Houston, Texas, evaluating the use of vadadustat as a potential therapy to prevent and lessen the severity of ARDS adult patients who have been hospitalized due to COVID-19. With the support of their data monitoring committee, UTHealth decided to expand their study beyond the initial 400 patients, an enrollment target they have now surpassed. Within this randomized, double-blind, placebo-controlled study, patients will be dosed with vadadustat or a placebo starting within 24 hours of hospital admission and continuing for up to 14 days. This study is being conducted under an Investigational New Drug application, or IND, with UTHealth as the study sponsor and is currently enrolling patients. In January of 2021, UTHealth announced that it had been awarded $5.1 million in funding from the U.S. Department of Defense, or DOD, to expand this clinical trial at its facilities.

- ***Auryxia*® *(ferric citrate)*** is approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with DD-CKD, or the Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with NDD-CKD, or the IDA Indication. Ferric citrate is also approved and marketed in Japan as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and for the treatment of patients with IDA, under the trade name Riona (ferric citrate hydrate). Since 2018, Auryxia product revenue has grown at a compounded annual growth rate of 14% due to market share gains and improved net price per pill, while total prescriptions for phosphate binders in the United States have declined 8%. We believe this growth is due to the benefits of the product perceived by the prescribing nephrologists as communicated by our nephrology-focused commercial and medical organizations.

If we obtain FDA approval of vadadustat, we plan to commercialize vadadustat in the United States with our well-established, nephrology-focused commercial organization, while also leveraging our collaboration with Otsuka and its U.S. nephrology commercial organization. In addition, in February 2022, we entered into a Second Amended and Restated License Agreement, or the Vifor Second Amended Agreement with Vifor (International) Ltd., or Vifor Pharma, which amended and restates the Amended and Restated License Agreement, dated April 8, 2019, or the Vifor First Amended Agreement. Pursuant to the Vifor Second Amended Agreement, we granted Vifor Pharma an exclusive license to sell vadadustat to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by us, to independent dialysis organizations that are members of group purchase organizations, and to certain non-retail specialty pharmacies in the United States, or the Territory. We refer to Fresenius Medical Care North America and its affiliates, these organizations and specialty pharmacies collectively as the “Supply Group". We currently retain rights to commercialize vadadustat for use in the non-dialysis dependent CKD market and to sell to dialysis organizations outside of the Supply Group. During the term of the Vifor Second Amended Agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the Territory to the Supply Group.

We market Auryxia in the United States with our well-established, nephrology-focused commercial organization. Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona in Japan. Auryxia is our only product approved for sale in the United States and it generated approximately $142.2 million in revenue from U.S. product sales during the year ended December 31, 2021.

In addition, we continue to explore additional development opportunities to expand our pipeline and portfolio of novel therapeutics through both internal research and external innovation. Our development pipeline includes several earlier stage opportunities, including praliciguat, an investigational oral soluble guanylate cyclase, or sGC, stimulator, that we licensed from Cyclerion Therapeutics, Inc., or Cyclerion, in June 2021. Praliciguat is in development for the treatment of focal segmental glomerulosclerosis, which is highly complementary of our strategy to identify and develop novel therapeutics for people impacted by kidney diseases.

Further, our internal innovation efforts include several preclinical opportunities, both in the HIF pathway, leveraging our learnings from the research and development of vadadustat, as well as new areas of focus we are currently exploring.

Operating Overview

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $282.8 million, $383.5 million and $279.7 million for the years ended December 31, 2021, 2020 and 2019, respectively. Substantially all of our net losses resulted from costs incurred in connection with the continued commercialization of Auryxia and development efforts relating to vadadustat, including conducting clinical trials of, and seeking regulatory approval for, vadadustat, providing general and administrative support for these operations and protecting our intellectual property.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on product

revenue, collaboration revenue, and our ability to obtain additional funding. We expect to continue to incur significant expenses if and as we:

- conduct and enroll patients in any clinical trials, including any post-marketing studies or any other clinical trials for Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- continue our commercialization activities for Auryxia and vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired,
- maintain marketing approvals for Auryxia, vadadustat, if approved, and any other product, including those that may be in-licensed or acquired;
- have Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, manufactured for clinical trials and for commercial sale;
- conduct discovery and development activities for additional product candidates or platforms that may lead to the discovery of additional product candidates;
- engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would market and develop commercial products, or develop and commercialize other product candidates and technologies;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract, hire and retain qualified personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- experience any delays or encounter issues with any of the above.

We have not generated, and may not generate, enough product revenue to realize net profits from product sales. We have no manufacturing facilities, and all of our manufacturing activities are contracted out to third parties. Additionally, we currently utilize contract research organizations, or CROs, to carry out our clinical development activities. If we obtain marketing approval for vadadustat, and as we continue to commercialize Auryxia, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We expect to finance future cash needs through product revenue, public or private equity or debt transactions, payments from our collaborators, royalty transactions, strategic transactions, or a combination of these approaches. If we are unable to raise additional capital in sufficient amounts when needed or on attractive terms, we may not be able to pursue development and commercial activities related to Auryxia and vadadustat, if approved, or any additional products and product candidates, including those that may be in-licensed or acquired. Any of these events could significantly harm our business, financial condition and prospects.

From inception through December 31, 2021, we raised approximately $792.7 million of net proceeds from the sale of equity, including $519.8 million from various underwritten public offerings, $222.9 million from at-the-market offerings, or ATM offerings, pursuant to sales agreements with Cantor Fitzgerald & Co., and $50.0 million from the sale of 3,571,429 shares of common stock to Vifor Pharma. During the year ended December 31, 2021, we raised $88.4 million of net proceeds from ATM offerings. At the inception of our collaboration agreements with Otsuka and MTPC, our collaborators committed to an aggregate of approximately $573.0 million or more in cost-share funding, which we generally continue to receive on a quarterly prepaid basis, and license payments. Of these commitments, we received approximately $272.0 million at the onset of the collaboration agreements. On November 11, 2019, we entered into a loan agreement, or the Loan Agreement, with funds managed by Pharmakon Advisors LP, or Pharmakon, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to us in two tranches, subject to certain terms and conditions, or the Term Loans. As of March 31, 2021, we had drawn down the full $100.0 million made available to us under the Loan Agreement. In addition, on February 25, 2021, we received an upfront payment of $44.8 million (net of certain transaction expenses) in connection with our sale to HealthCare Royalty Partners IV, L.P., or HCR, of the right to receive all royalties and sales milestones payable to us under our collaboration agreement with MTPC, or the MTPC Agreement, subject to certain caps and other terms and conditions described in Note 4 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

Impacts of COVID-19 Pandemic

The ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, pandemic has presented a substantial public health and economic challenge around the world and continues to affect our employees, patients, healthcare providers with whom we interact, customers, collaboration partners, CROs, contract manufacturing organizations, or CMOs, vendors, communities and business operations. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition continues to depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning the COVID-19 pandemic, any resurgences or variants of COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets where the healthcare providers with whom we interact, our partners, our CROs, our CMOs, and our other vendors operate.

We believe our revenue growth was negatively impacted during 2021 primarily as the CKD patient population that we serve continue to experience both higher hospitalization and mortality rates due to COVID-19. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, COVID-19 continues to adversely and disproportionately impact CKD patients; therefore, we expect COVID-19 to continue to have a negative impact on our revenue growth for the foreseeable future.

The majority of our office-based employees began working from home in March 2020, and continue to primarily work from home. While most of our office-based operations can be performed remotely, there is no guarantee that we will continue to be as effective while working remotely because our team is dispersed, which has limited valuable in-person employee team interactions, and employees may become sick themselves and be unable to work. Further, our increased reliance on remote access to our information systems increases our exposure to potential cybersecurity breaches.

Moreover, our future success and profitability substantially depends on the management skills of our executives and certain other key employees. The unanticipated loss or unavailability of key employees due to the pandemic could harm our ability to operate our business or execute our business strategy and we may not be successful in finding and integrating suitable successors in the event of key employee loss or unavailability. For example, as of January 1, 2022, we have required all of our employees be fully vaccinated, subject to limited medical and religions exemptions in accordance with applicable laws. At this time, it is not possible to predict with certainty the exact impact that our vaccine requirement will continue to have on us or on our workforce. The vaccine requirement has resulted, and may continue to result, in employee distraction and could result in litigation and difficulty securing future labor needs. This could have an adverse effect on our business, results of operations and cash flows.

In addition, several healthcare facilities have previously restricted access for non-patients, including the members of our sales force. For example, DaVita, Inc., or DaVita, and Fresenius Medical Care, or Fresenius, which account for a vast majority of the dialysis population in the United States, have previously restricted access to their clinics. As a result, we continue to engage with some healthcare providers and other customers virtually, where possible. The restrictions on our customer-facing employees' in-person interactions with healthcare providers could negatively impact our access to healthcare providers and, ultimately, our sales, including with respect to vadadustat, if approved. Recently, such precautionary measures have been relaxed at certain healthcare facilities and, as a result, members of our sales force have resumed in person interactions with certain customers. Nevertheless, some restrictions remain, and more restrictions may be put in place again due to a resurgence in COVID-19 cases, including those involving new variants of COVID-19 which may be more contagious and more severe than prior strains of the virus. Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand for Auryxia, and will be for vadadustat, if approved, including the potential for further declines or changes in prescription trends and customer orders.

In addition, the direct and indirect impacts of the pandemic or the response efforts to the pandemic, including, among others, competition for labor and resources and increases in labor, sourcing, manufacturing and shipping costs, may cause disruptions to, closures of or other impacts on our CMOs and other vendors in our supply chain on which we rely for the supply of our products and product candidates. At this time, our third party contract manufacturers continue to operate at or near normal levels. However, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our contract manufacturers' ability to manufacture and deliver Auryxia and vadadustat (if approved in the United States and which is currently marketed under the trade name Vafseo™ by MTPC in Japan), which may result in increased costs and delays, or disruptions to manufacturing and supply of our products and product candidates and have a negative effect on our inventory reserves, which could result in an increase in inventory write-offs due to expiry.

COVID-19 pandemic precautions have caused moderate delays in enrolling new clinical trials and may cause delays in enrolling other new clinical trials. We are using remote monitoring and central monitoring, where possible.

This uncertain COVID-19 pandemic environment has presented new risks to our business. While we are working to mitigate the impacts on our business, we are mindful that many of these risks and the impact to the larger healthcare market are outside of our control.

For additional information on the various risks posed by the COVID-19 pandemic, please refer to Part I, Item 1A. Risk Factors.

Financial Overview

Revenue

To date, our revenues have been derived from collaboration revenues, which include license and milestone payments, royalty and cost-sharing revenue generated through collaboration and license agreements with partners for the development and commercialization of vadadustat and, following the Merger, commercial sales of Auryxia and royalty revenue from sales of Riona in Japan. Cost-sharing revenue represents amounts reimbursed by our collaboration partners for expenses incurred by us for research and development activities and, potentially, co-promotion activities, under our collaboration agreements.

We expect our revenue to continue to be generated primarily from our collaborations with Otsuka and MTPC and any other collaborations into which we may enter, as well as commercial sales of Auryxia and vadadustat, if approved, in the United States, and royalty revenue from JT and Torii, based on net sales of Riona in Japan.

Cost of Goods Sold

Cost of goods sold includes direct costs to manufacture commercial drug substance and drug product for Auryxia, as well as indirect costs, including costs for packaging, shipping, insurance and quality assurance, idle capacity charges, write-offs for inventory that fails to meet specifications or is otherwise no longer suitable for commercial sale, changes in our excess purchase commitment liability, and royalties due to the licensor of Auryxia related to the U.S. product sales recognized during the period. Cost of goods sold also includes costs to manufacture drug product provided to MTPC for commercial sale of Vafseo in Japan.

As a result of the Merger and the application of purchase accounting, costs of goods sold also includes both amortization expense and, if applicable, impairment charges associated with the fair value of the developed product rights for Auryxia as well as expense associated with the fair value inventory step-up. The fair value of the developed product rights for Auryxia is being amortized over its estimated useful life, which as of December 31, 2021 is estimated to be six years. The fair value inventory step-up as a result of the Merger was fully amortized as of the first quarter of 2021.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of vadadustat, which include:

- personnel-related expenses, including salaries, benefits, recruiting fees, travel and stock-based compensation expense of our research and development personnel;
- expenses incurred under agreements with CROs and investigative sites that conduct our clinical trials;
- the cost of acquiring, developing and manufacturing clinical study materials through CMOs;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies;
- costs associated with preclinical, clinical and regulatory activities; and
- costs associated with vadadustat pre-launch inventory build, which remains subject to approval in the United States.

Research and development costs are expensed as incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We cannot determine with certainty the duration and completion costs of current or future clinical trials of Auryxia and vadadustat or if, when, or to what extent we will generate revenue from the commercialization and sale of vadadustat, if approved. We may never succeed in achieving marketing approval for vadadustat.

The duration, costs and timing of clinical trials and development of Auryxia and vadadustat will depend on a variety of factors including, but not limited to, those described in Part I, Item 1A. Risk Factors. A change in the outcome of any of these variables with respect to the development of Auryxia and vadadustat could mean a significant change in the costs and timing associated

with that development. For example, if the FDA, the EMA, or other regulatory authorities were to require us to conduct clinical trials in addition to or different from those that we currently anticipate, or if we experience delays in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

From inception through December 31, 2021, we have incurred $1.4 billion in research and development expenses. We expect to have significant research and development expenditures for the foreseeable future as we continue the development of Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired.

Our direct research and development expenses consist principally of external costs, such as fees paid to clinical trial sites, consultants, central laboratories and CROs in connection with our clinical trials, and drug substance and drug product manufacturing for clinical trials.

In 2020, we completed our global Phase 3 clinical program for vadadustat to which the majority of our research and development costs are attributable. A significant portion of our research and development costs have been external costs, which we track on a program-by-program basis. These external costs include fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical trials, and costs related to acquiring and manufacturing clinical trial materials. Our internal research and development costs are primarily personnel-related costs, depreciation and other indirect costs. We do not track our internal research and development expenses on a program-by-program basis as they are deployed across multiple projects under development.

The following table summarizes our external research and development expenses by program, as well as expenses not allocated to programs, for the years ended December 31, 2021 and 2020:

	Year ended December 31,	
	2021	2020
	(in thousands)	
Vadadustat external costs	$ 48,506	$ 128,869
External costs for other programs	25,907	15,020
Total external research and development expenses	74,413	143,889
Headcount, consulting, facilities and other	73,439	74,596
Total research and development expenses	$ 147,852	$ 218,485

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses for our commercial personnel, including our field sales force and other commercial support personnel, as well as personnel in executive and other administrative or non-research and development functions. Other selling, general and administrative expenses include facility-related costs, fees for directors, accounting and legal services fees, recruiting fees and expenses associated with obtaining and maintaining patents.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

	Year ended December 31,		
	2021	2020	Increase (Decrease)
		(In Thousands)	
Revenues:			
Product revenue, net	$ 142,216	$ 128,901	$ 13,315
License, collaboration and other revenue	71,362	166,406	(95,044)
Total revenues	213,578	295,307	(81,729)
Cost of goods sold:			
Product	117,352	148,866	(31,514)
Amortization of intangibles	36,042	31,515	4,527
Impairment of intangible asset	—	115,527	(115,527)
Total cost of goods sold	153,394	295,908	(142,514)
Operating expenses:			
Research and development	147,852	218,485	(70,633)
Selling, general and administrative	174,161	153,947	20,214
License expense	3,489	3,409	80
Total operating expenses	325,502	375,841	(50,339)
Operating loss	(265,318)	(376,442)	111,124
Other expense, net	(17,522)	(7,015)	(10,507)
Net loss before income taxes	(282,840)	(383,457)	100,617
Benefit from income taxes	—	—	—
Net loss	$ (282,840)	$ (383,457)	$ 100,617

Product Revenue, Net. Net product revenue is derived from sales of our only commercial product in the United States, Auryxia. We distribute our product principally through a limited number of wholesale distributors as well as certain specialty pharmacy providers. Net product revenue was $142.2 million for the year ended December 31, 2021, compared to net product revenue of $128.9 million for the year ended December 31, 2020. The increase was primarily due to an increase in units sold and improved payer mix, partially offset by the negative impact from COVID-19 on our revenues during 2021. We believe our revenue growth continues to be negatively impacted primarily as the CKD patient populations that we serve continue to experience both higher hospitalization and mortality rates due to COVID-19.

As an oral drug, Auryxia is covered by Medicare only under Part D. However, in September 2018, CMS decided that Auryxia would no longer be covered by Medicare for the IDA Indication. While this decision does not impact CMS coverage of the Hyperphosphatemia Indication, it requires Part D plan sponsors to impose prior authorization or other steps to ensure that Auryxia is used only for the Hyperphosphatemia Indication. However, due to the COVID-19 pandemic, CMS has issued a guidance that expressly encouraged Part D plans to waive all prior authorization requirements. This guidance was issued in March of 2020 and updated in May of 2020. In both versions of the guidance, CMS clarified that due to COVID-19, Part D plan sponsors are encouraged to waive prior authorization requirements.

Further, on October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts against CMS and the U.S. Department of Health and Human Services challenging CMS's decision that Auryxia would no longer be covered by Medicare for the IDA Indication and imposing a prior authorization requirement for Auryxia in the Hyperphosphatemia Indication, or the CMS Decision. On October 22, 2021, the parties agreed to dismiss the litigation. See Part I, Item 3. Legal Proceedings for further information. While we believe that the vast majority of the Medicare prescriptions written for Auryxia today are for the Hyperphosphatemia Indication and therefore will continue to be covered by Medicare with prior authorization, the CMS Decision has had and will continue to have an adverse impact on the sales and future growth of Auryxia for the Hyperphosphatemia Indication and the IDA Indication.

License, Collaboration and Other Revenue. License, collaboration and other revenue was $71.4 million for the year ended December 31, 2021, compared to $166.4 million for the year ended December 31, 2020. We recognized $65.5 million in collaboration revenue for the year ended December 31, 2021 from our cost sharing arrangement under the Otsuka collaboration agreement for the United States, or the Otsuka U.S. Agreement, and the Otsuka collaboration agreement for certain territories outside the United States, or the Otsuka International Agreement, and royalty revenue earned under our collaboration agreement with MTPC, or the MTPC Agreement. We recognized $154.3 million in collaboration revenue for the year ended December 31,

2020 from our cost sharing arrangement under the Otsuka U.S. Agreement and the Otsuka International Agreement and recognition of a milestone and royalty revenue under the MTPC Agreement. The decrease in collaboration revenue was driven by lower payments recognized under both the Otsuka U.S. Agreement and the Otsuka International Agreement as we completed our global Phase 3 clinical development program for vadadustat in 2020 and are currently engaged in close-out activities with respect to the program.

Cost of Goods Sold - Product. Cost of goods sold of $117.4 million for the year ended December 31, 2021 primarily consisted of costs associated with the manufacturing of Auryxia and supply of Vafseo to MTPC for commercial sale in Japan, $33.4 million in non-cash charges related to our excess purchase commitment liability, $21.6 million in non-cash charges related to the fair-value inventory step-up from the application of purchase accounting, and $15.6 million primarily related to excess and obsolescence reserves associated with Auryxia as well as inventory reserves associated with a previously disclosed manufacturing quality issue related to Auryxia. See Note 14 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K for further details of the increase to the liability for excess purchase commitments.

Cost of goods sold of $148.9 million for the year ended December 31, 2020 primarily consisted of costs associated with the manufacturing of Auryxia, $68.2 million in non-cash charges related to the fair-value inventory step-up from the application of purchase accounting, $25.1 million in non-cash charges related to an increase in the liability for excess purchase commitments, and $20.1 million primarily related to the write-down of inventory associated with specific lots of Auryxia because it was determined that these lots were not manufactured in conformance with the FDA's GMP guidance relating to validation.

Cost of Goods Sold - Amortization of Intangibles. Amortization of intangibles relates to the acquired developed product rights for Auryxia. Amortization of intangibles during the years ended December 31, 2021 and 2020 was $36.0 million and $31.5 million, respectively. The increase in amortization charges is due to the prospective adjustment of the estimated useful life of the developed product rights for Auryxia from seven years to six years that occurred in the fourth quarter of 2020.

Cost of Goods Sold - Impairment of Intangible Asset. In the second quarter of 2020, in connection with a routine business review, we reduced our short-term and long-term Auryxia revenue forecast. This reduction was primarily driven by the compounding impact of the CMS Decision that rescinded Medicare Part D coverage of Auryxia for the IDA Indication, and imposed a prior authorization requirement for Auryxia for the Hyperphosphatemia Indication. As a result, we recorded an impairment charge of $115.5 million to the Auryxia intangible asset during the year ended December 31, 2020. There were no such impairment charges during the year ended December 31, 2021.

Research and Development Expenses. Research and development expenses were $147.9 million for the year ended December 31, 2021, compared to $218.5 million for the year ended December 31, 2020. The net decrease of $70.6 million was due to the following:

	(in millions)
Vadadustat external development expenses	(80.4)
Other external research and development	10.9
Headcount, consulting and facilities	(1.1)
Total net decrease	$ (70.6)

The decrease in the costs related to the development of vadadustat is primarily attributable to a decrease in external costs related to our global Phase 3 program (INNO$_2$VATE and PRO$_2$TECT), for which we reported top-line data in the second and third quarters of 2020, respectively. Although we expect our research and development expenses to continue to decrease in the near term as we completed our global Phase 3 clinical development program for vadadustat in 2020, we will continue to incur significant research and development expenses in future periods in support of ongoing or planned studies with respect to Auryxia and vadadustat and development of other potential product candidates.

Selling, General and Administrative Expenses. Selling, general and administrative expenses were $174.2 million for the year ended December 31, 2021, compared to $153.9 million for the year ended December 31, 2020. The increase of $20.2 million was primarily due to higher marketing expenses, increased headcount related costs, and one-time legal costs. In 2022, we expect our selling, general and administrative expenses for our ongoing commercialization of Auryxia and for support of our potential commercialization of vadadustat to increase modestly from 2021.

License Expenses. License expense related to royalties due to Panion relating to sales of Riona in Japan were $3.5 million and $3.4 million for the years ended December 31, 2021 and 2020, respectively.

Other Expense, Net. Other expense, net, was $17.5 million for the year ended December 31, 2021, compared to $7.0 million for the year ended December 31, 2020. The increase was primarily due to $9.1 million in non-cash interest expense on the liability related to the sale of our right to receive royalties and sales milestones from MTPC as further described in Note 5 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K as well as interest expense associated with our Term Loans. Other expense, net for the year ended December 31, 2020 was primarily due to interest expense associated with our Term Loans.

Comparison of the Years Ended December 31, 2020 and 2019

For discussion of our 2020 results and a comparison with 2019 results please refer to Part II, Item 7, "Management's Discussion and Analysis of Financial Conditions and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 that was filed with the SEC on February 25, 2021, or the 2020 Form 10-K.

Liquidity and Capital Resources

We have funded our operations principally through sales of our common stock, payments received from our collaboration partners and, following the Merger, product sales, debt and a royalty transaction. As of December 31, 2021, we had cash and cash equivalents of approximately $149.8 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. At inception of our collaboration agreements with Otsuka and MTPC, our collaborators committed to an aggregate of approximately $573.0 million or more in cost-share funding, of which we received approximately $272.0 million at the onset of the collaborations, as further described in Note 4 contained in this Annual Report on Form 10-K and the remainder of which we will generally continue to receive on a quarterly prepaid basis, and through license payments.

Cash Flows

The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	Year ended December 31,		
	2021	2020	2019
		(In Thousands)	
Net cash provided by (used in):			
Operating activities	$ (252,965)	$ (110,388)	$ (257,441)
Investing activities	39,941	(40,004)	211,176
Financing activities	133,731	231,720	88,970
Net increase in cash, cash equivalents and restricted cash	$ (79,293)	$ 81,328	$ 42,705

Operating Activities. Net cash used in operating activities during the year ended December 31, 2021 of $253.0 million was largely driven by payroll-related expenses, rebate payments and payments for inventory. These payments were partially offset by adjustments for non-cash items, including amortization of intangibles of $36.0 million, increases to the liability for excess purchase commitments of $33.4 million, stock-based compensation expense of $22.7 million, fair value step-up of inventory sold or written off of $21.6 million, write-downs of inventory of $15.6 million, and non-cash interest expense related to the sale of future royalties of $9.1 million.

Net cash used in operating activities during the year ended December 31, 2020 of $110.4 million was largely driven by timing of payments on our Phase 3 development program for vadadustat, payments for inventory and merger-related liabilities. These payments were partially offset by adjustments for non-cash items, including the intangible asset impairment charge of $115.5 million, the fair value write-up of inventory sold or written off of $68.2 million, amortization of intangibles of $31.5 million, increases to the liability for excess purchase commitments of $25.1 million, stock-based compensation expense of $24.5 million, and write-downs of inventory of $20.1 million primarily associated with specific lots of Auryxia because it was determined that these lots were not manufactured in conformance with the FDA's GMP guidance relating to validation.

Investing Activities. Net cash provided by investing activities during the year ended December 31, 2021 of $39.9 million was comprised of proceeds from the maturities of available for sale securities of $40.0 million, partially offset by immaterial purchases of equipment.

Net cash used in investing activities during the year ended December 31, 2020 of $40.0 million was comprised primarily of purchase of available for sale securities of $99.9 million, partially offset by proceeds from the maturities of available for sale securities of $60.2 million.

Financing Activities. Net cash provided by financing activities for the year ended December 31, 2021 was $133.7 million and consisted of net proceeds from the sale of future royalties of $44.8 million, net proceeds from the public issuance of common stock in connection with our ATM sales agreement of $88.2 million, and proceeds from the sale of stock under our employee stock purchase plan.

Net cash provided by financing activities for the year ended December 31, 2020 was $231.7 million and consisted of net proceeds from the public issuance of common stock in connection with our ATM sales agreement of $209.4 million, proceeds from the issuance of debt of $20.0 million, and proceeds from the exercise of stock options and from the sale of stock under our employee stock purchase plan.

A discussion of changes in our cash flow from the year ended December 31, 2019 to the year ended December 31, 2020 can be found in Part II, Item 7, "Management's Discussion and Analysis of Financial Conditions and Results of Operations" of the 2020 Form 10-K.

Operating Capital Requirements and Going Concern

We have one product, Auryxia, approved for commercial sale in the United States and one product candidate, vadadustat, subject to FDA approval in the U.S., but have not generated, and may not generate, enough product revenue from the sale of Auryxia or sales of vadadustat, if approved, to realize net profits from product sales. We have incurred losses and cumulative negative cash flows from operations since our inception in February 2007, and as of December 31, 2021, we had an accumulated deficit of $1.5 billion. We anticipate that we will continue to incur losses for the foreseeable future, and we expect to continue to incur additional research and development and selling, general and administrative expenses for our ongoing research and development and potential commercialization of vadadustat and our ongoing development and commercialization of Auryxia.

We expect our cash resources to fund our current operating plan for at least twelve months from the date of this filing. However, the potential timely regulatory approval of vadadustat and the receipt of associated regulatory milestones and product revenues are an important source of funding of our cash runway, which are outside of our control. We expect to finance future cash needs through product revenue, public or private equity or debt transactions, payments from our collaborators (including associated regulatory approval milestones), royalty transactions, strategic transactions, or a combination of these approaches. In any event, we will require additional funding to fund our strategy and operating plan beyond the next twelve months, including to pursue development and commercial activities related to Auryxia and vadadustat, if approved, or any additional products and product candidates, including those that may be in-licensed or acquired. If we are unable to obtain sufficient funding, we could be required to delay our development efforts, limit activities and reduce costs, which could adversely affect our business prospects. There can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, or that its cash resources will fund our operating plan for the period anticipated by us or that additional funding will be available on terms acceptable to us, or at all.

In addition, on February 18, 2022, we entered into the First Amendment and Waiver with BioPharma Credit PLC, or the Collateral Agent, BPCR Limited Partnership, as a Lender, and BioPharma Credit Investments V (Master) LP, as a Lender, or the First Amendment and Waiver, which amends and waives certain provisions of the Loan Agreement, dated November 11, 2019. The Collateral Agent and the lenders are collectively referred to as Pharmakon (see Note 18). Pursuant to the covenants in the Loan Agreement, as amended, our Quarterly Reports on Form 10-Q for the fiscal quarters ending June 30, 2022 and September 30, 2022 and our future Annual Reports on Form 10-K must not be subject to any qualification as to going concern. If any of these filings are subject to any qualification related to going concern, it will result in an event of default under the Loan Agreement. If an event of default occurs and is continuing under the Loan Agreement, the Collateral Agent is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement, which we may not have the available cash resources to repay at such time. Should we not be able to meet the quarterly or annual covenants in the future, we would seek a waiver of this provision. However, there can be no assurances that we would be successful in obtaining such waiver.

Going Concern

Because the potential timely regulatory approval of vadadustat and the receipt of associated regulatory milestones and product revenues are outside of our control, there is uncertainty as to whether or not we will meet our quarterly and annual debt covenants. The conditions above, including the going concern covenants in our Loan Agreement, raise substantial doubt regarding our ability to continue as a going concern for a period of one year after the date the financial statements are issued.

Management's plans to alleviate the conditions that raise substantial doubt include raising additional funding through the sources detailed above for us to continue as a going concern for a period of twelve months from the date the financial statements are issued. We have concluded that the likelihood that our plan to obtain sufficient funding from one or more of these sources will be successful, while reasonably possible, is less than probable. Accordingly, we have concluded that substantial doubt exists about our ability to continue as a going concern for a period of at least twelve months from the date of issuance of these financial statements.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves numerous risks and uncertainties, and actual results could vary as a result of a number of factors, many of which are outside our control. We have based this estimate on assumptions that may be substantially different than actual results, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both near- and long-term, will depend on many factors including, but not limited to, those described under Part I, Item 1A. Risk Factors under the heading "Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy."

Contractual Obligations and Commitments

Leases

We lease approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts under a lease which was most recently amended in November 2020, collectively the Cambridge Lease. Under the Third Amendment to the Cambridge Lease, or the Third Amendment, executed in July 2016, total monthly lease payments under the initial base rent were approximately $242,000 and are subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises commenced on January 1, 2017 in the monthly amount of approximately $22,000. The Fourth Amendment to the Cambridge Lease, executed in May 2017, provided additional storage space to us and did not impact rent payments. In April 2018, we entered into a Fifth Amendment to the Cambridge Lease, or the Fifth Amendment, for an additional 19,805 square feet of office space on the 12th floor. Monthly lease payments for the existing 45,362 square feet of office and lab space, under the Third Amendment, remain unchanged. The new space leased by us was delivered in September 2018 and additional monthly lease payments of approximately $135,000 commenced in February 2019 and are subject to annual rent escalations, which commenced in September 2019. In November 2020, we entered into a Sixth Amendment to the Cambridge Lease, or the Sixth Amendment, to extend the term of the Cambridge Lease with respect to the lab space from November 30, 2021 to January 31, 2025. The Sixth Amendment includes two months of free rent starting in December 2020 and additional monthly lease payments of approximately $48,000 which commenced in December 2021, and is subject to annual rent escalations, which commence in December 2022.

Additionally, as a result of the Merger, we have a lease for 27,300 square feet of office space in Boston, Massachusetts, or the Boston Lease, which expires on February 28, 2023. The total monthly lease payments under the base rent are approximately $136,000 and are subject to annual rent escalations. On February 24, 2022, we entered into a First Amendment to Lease, or the First Lease Amendment, with CLPF One Marina Park Drive LLC (successor-in-interest to Fallon Cornerstone One MPD LLC), or the Landlord, amending the Boston Lease. Pursuant to the First Lease Amendment, we agreed to extend the term of the Boston Lease until July 31, 2031. The monthly lease payment pursuant to the First Amendment will be $200,122 commencing on August 1, 2023 and subject to annual rent escalation of approximately 2% commencing on August 1, 2024. The First Lease Amendment also includes a Landlord's allowance for certain leasehold improvements to the Premises in an amount of up to $1,954,680, provided that such allowance must be used prior to August 1, 2024. See Note 18 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K for more information.

In September 2019, Keryx entered into an agreement to sublease the Boston office space to Foundation Medicine, Inc., or Foundation. The sublease is subject and subordinate to the Boston Lease between Keryx and the landlord. The term of the sublease commenced on October 16, 2019, upon receipt of the required consent from the landlord for the sublease agreement, and expires on February 27, 2023. Foundation is obligated to pay Keryx rent that approximates the rent due from us to Keryx's landlord with respect to the Boston Lease. Keryx continues to be obligated for all payment terms pursuant to the Boston Lease, and we will guaranty Keryx's obligations under the sublease.

Term Loans

On November 11, 2019, Akebia, with Keryx as guarantor, entered into a loan agreement, or the Loan Agreement, with BioPharma Credit PLC as collateral agent and a lender, or the Collateral Agent, and BioPharma Credit Investments V (Master) LP as a lender, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to us in two tranches, subject to certain terms and conditions, or the Term Loans. BioPharma Credit PLC subsequently transferred its interest in the Term Loans, solely in its capacity as a lender, to its affiliate, BPCR Limited Partnership. The Collateral Agent

and the lenders are collectively referred to as Pharmakon. The first tranche of $80.0 million, or Tranche A, was drawn on November 25, 2019, or the Tranche A Funding Date, and the second tranche of $20.0 million, or Tranche B, was drawn on December 10, 2020, or the Tranche B Funding Date. A more detailed description of the term loans can be found in Note 11 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K. On February 18, 2022, in connection with entering into the Vifor Second Amended Agreement, we, BioPharma Credit PLC, or the Collateral Agent, BPCR Limited Partnership, as a Lender, and BioPharma Credit Investments V (Master) LP, as a Lender, entered into the First Amendment and Waiver, which amends and waives certain provisions of the Loan Agreement, dated November 11, 2019, between the parties. See Note 18 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K for more information.

Manufacturing Agreements

As a result of the Merger, our contractual obligations include Keryx's commercial supply agreements with BioVectra Inc., or BioVectra, and Siegfried Evionnaz SA, or Siegfried, to supply commercial drug substance for Auryxia.

Pursuant to the Manufacture and Supply Agreement with BioVectra and the Product Manufacture and Supply and Facility Construction Agreement with BioVectra, we agreed to purchase minimum quantities of Auryxia drug substance annually at predetermined prices. On September 4, 2020, we and BioVectra entered into an Amended and Restated Product Manufacture and Supply and Facility Construction Agreement, which provided for reduced minimum quantity commitments and revised the predetermined prices. The price per kilogram decreases with an increase in quantity above the predetermined purchase quantity tiers. In addition, the Manufacture and Supply Agreement with BioVectra and the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement with BioVectra, requires us to reimburse BioVectra for certain costs in connection with construction of a new facility for the manufacture and supply of Auryxia drug substance. These construction costs are recorded in other assets and amortized into drug substance as inventory is released to us from BioVectra. The term of the Manufacture and Supply Agreement with BioVectra expires on December 31, 2022. The term of the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement expires on December 31, 2026, after which, it automatically renews for successive one-year terms unless either party gives notice of its intention to terminate within a specified time prior to the end of the then-current term. In addition, we and BioVectra each have the ability to terminate these agreements upon the occurrence of certain conditions. As of December 31, 2021, we are required to reimburse BioVectra for certain costs in connection with the construction of the new facility and to purchase minimum quantities of Auryxia drug substance annually for a total cost of approximately $83.6 million through the end of the contract term.

Pursuant to the Siegfried Master Manufacturing Services and Supply Agreement, as amended (the most recent amendment having been executed on February 11, 2021), or the Siegfried Agreement, we have agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The term of the Siegfried Agreement expires on December 31, 2022, subject to our option to extend the term through December 31, 2023, by providing 12 months' prior written notice to Siegfried. As of the date of the filing of this Annual Report on Form 10-K, we have notified Siegfried that we have elected not to exercise our option to extend the term of the Siegfried Agreement through December 31, 2023. In addition, the Siegfried Agreement provides us and Siegfried with certain early termination rights. As of December 31, 2021, we are required to purchase a minimum quantity of drug substance under the Siegfried Agreement for Auryxia annually at a total cost of approximately $15.6 million through the year ending December 31, 2022.

As part of purchase accounting, we identified executory contracts in the commercial supply agreements between Keryx and its contract manufacturers for Auryxia, which include future firm purchase commitments. These executory contracts were deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast. The liability related to the amount of purchase commitments that exceed the current forecast was $76.7 million and $55.8 million as of December 31, 2021 and 2020, respectively. The $20.9 million increase in liability, which was driven by reductions in the short-term and long-term Auryxia revenue sales forecast and related estimates of expiry during the year ended December 31, 2021 partially offset by a decrease due to inventory received that had been previously reserved within the excess purchase commitment liability and a reduction in commitments related to an amendment to the Siegfried Agreement during the year ended December 31, 2021. The increase in the liability was recorded to cost of goods sold.

On April 9, 2019, we entered into a Supply Agreement with Esteve Química, S.A., or Esteve, or the Esteve Agreement. The Esteve Agreement includes the terms and conditions under which Esteve will manufacture vadadustat drug substance for commercial use. Pursuant to the Esteve Agreement, we provide rolling forecasts to Esteve on a quarterly basis, or the Esteve Forecast. The Esteve Forecast reflects our needs for vadadustat drug substance produced by Esteve over a certain number of months, represented as a quantity of vadadustat drug substance per calendar quarter. The parties have agreed to a volume-based pricing structure under the Esteve Agreement. The Esteve Agreement has an initial term of four years, beginning April 9, 2019 and ending April 9, 2023. Pursuant to the Esteve Agreement, we have agreed to purchase a certain percentage of the global

demand for vadadustat drug substance from Esteve. As of December 31, 2021, we have committed to purchase $28.9 million of vadadustat drug substance from Esteve through the fourth quarter of 2022.

On March 11, 2020, we entered into a Supply Agreement with Patheon Inc., or Patheon, or the Patheon Agreement. The Patheon Agreement includes the terms and conditions under which Patheon will manufacture vadadustat drug product for commercial use. Pursuant to the Patheon Agreement, we provide Patheon a long-term forecast on an annual basis, as well as short-term forecasts on a quarterly basis, or the Patheon Forecast. The Patheon Forecast reflects our needs for commercial supply of vadadustat drug product produced by Patheon, represented as a quantity of drug product per calendar quarter. The parties have agreed to a volume-based pricing structure under the Patheon Agreement. The Patheon Agreement has an initial term beginning March 11, 2020 and ending June 30, 2023. Pursuant to the Patheon Agreement, we have agreed to purchase a certain percentage of the global demand for vadadustat drug product from Patheon. As of December 31, 2021, we had a minimum commitment with Patheon for $4.0 million through the fourth quarter of 2022.

On April 2, 2020, we entered into a Supply Agreement with STA Pharmaceutical Hong Kong Limited, a subsidiary of WuXi AppTec, or WuXi STA, as amended on April 15, 2021, or the WuXi STA DS Agreement. The WuXi STA DS Agreement includes the terms and conditions under which WuXi STA will manufacture vadadustat drug substance for commercial use. Pursuant to the WuXi STA DS Agreement, we provide rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DS Forecast. The WuXi STA DS Forecast reflects our needs for vadadustat drug substance produced by WuXi STA over a certain number of quarters. The parties have agreed to a volume-based pricing structure under the WuXi STA DS Agreement. The WuXi STA DS Agreement has an initial term of four years, beginning April 2, 2020 and ending April 2, 2024. Pursuant to the WuXi STA DS Agreement, we have agreed to purchase a certain percentage of the global demand for vadadustat drug substance from WuXi STA. As of December 31, 2021, we have committed to purchase $29.2 million of vadadustat drug substance from WuXi STA through the third quarter of 2022.

On February 10, 2021, we entered into a Supply Agreement with WuXi STA, or the WuXi STA DP Agreement. The WuXi STA DP Agreement includes the terms and conditions under which WuXi STA will manufacture and supply vadadustat drug product for commercial purposes. Pursuant to the WuXi STA DP Agreement, we will provide rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DP Forecast. Each WuXi STA DP Forecast will reflect the quantities of vadadustat drug product that we expect to order from WuXi STA over a certain number of months, represented as a quantity of vadadustat drug product per calendar quarter. Pursuant to the WuXi STA DP Agreement, we have agreed to purchase a certain percentage of global demand for vadadustat drug product from WuXi STA. The parties have agreed to a volume-based pricing structure under the WuXi STA DP Agreement. The vadadustat drug product price will remain fixed for the first 12 months and thereafter shall be annually reviewed by us and WuXi STA. We will also reimburse WuXi STA for certain reasonable expenses. The WuXi STA DP Agreement has an initial term of four years, beginning February 10, 2021 and ending February 10, 2025. The WuXi STA DP Agreement may be renewed or extended by mutual agreement of us and WuXi STA with at least 18 months' prior written notice. The WuXi STA DP Agreement allows us to terminate the relationship on 180 calendar days' prior written notice to WuXi STA for any reason. In addition, each party has the ability to terminate the WuXi STA DP Agreement upon the occurrence of certain conditions.

Other Third Party Contracts

Under our agreement with IQVIA to provide contract research organization services for the PRO_2TECT and $INNO_2VATE$ programs, the total remaining contract costs as of December 31, 2021 were approximately $5.0 million, of which Otsuka reimburses a significant portion back to us. Substantive performance for the committed work with IQVIA was completed in 2020 and close out activities were performed throughout 2021 and will continue to be performed throughout 2022. We also contract with various other organizations to conduct research and development activities with remaining contract costs to us of approximately $237.8 million as of December 31, 2021. The scope of the services under these research and development contracts can be modified and the contracts cancelled by us upon written notice, and therefore not included in the table of contractual obligations and commitments. In some instances, the contracts may be cancelled by the third party upon written notice.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue, inventory, our excess purchase commitment liability, liabilities related to sale of future royalties, impairment of intangible assets, and income

taxes. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Product Revenue, Net

We sell Auryxia in the United States, primarily to wholesale distributors as well as certain specialty pharmacy providers, collectively, Customers. These Customers resell our product to health care providers and patients. In addition to distribution agreements with Customers, we enter into arrangements with health care providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks, and discounts with respect to the purchase of our product.

We recognize revenue on product sales when the Customer obtains control of our product, which occurs at a point in time, typically upon delivery to the Customer. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less.

Revenue from product sales is recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and are based on various incentives that are offered within contracts between us and our Customers, health care providers, payors and other indirect customers relating to sales of our products. These reserves are based on the amounts earned or to be claimed on the related sales. These reserves include:

- Trade Discounts and Allowances: Discounts that include incentive fees that are explicitly stated in our contracts. In addition, we compensate (through trade discounts and allowances) our Customers for sales order management, data, and distribution services.
- Product Returns: Consistent with industry practice, we generally offer Customers a limited right of return which allows for the product to be returned when the product expiry is within an allowable window, when the quantity delivered is different than quantity ordered, the product is damaged in transit prior to receipt by the customer, or is subject to a recall. This right of return generally lapses once the product is provided to a patient. We estimate the amount of our product sales that may be returned for credit by our Customers. We currently estimate product return reserve using available industry data and our own historical sales information, including our visibility into the inventory remaining in the distribution channel.
- Provider Chargebacks and Discounts: Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. Reserves for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel at each reporting period end that we expect will be sold to qualified healthcare providers, and chargebacks that Customers have claimed but for which we have not yet issued a credit.
- Commercial and Medicare Part D Rebates: We contract with various commercial payor organizations, primarily health insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of our products. We estimate the rebates for commercial and Medicare Part D payors based upon (i) our contracts with the payors and (ii) information obtained from our Customers and other third parties regarding the payor mix for Auryxia.
- Other Government Rebates: We are subject to discount obligations under state Medicaid programs and other government programs. We estimate Medicaid and other government programs rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.
- Other Incentives: Other incentives that we offer include voluntary patient assistance programs such as our co-pay assistance program, which are intended to provide financial assistance to qualified commercially insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on actual claims processed during a given period, as well as historical utilization data to estimate the amount we expect to receive associated with product that has been recognized as revenue, but remains in in the distribution channel at the end of each reporting period.

When appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying

and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the respective underlying contracts.

The preceding estimates and judgments materially affect our recognition of net product revenues. Changes in our estimates of net product revenues could have a material effect on net product revenues recorded in the period in which we determine that change occurs.

Collaboration Revenues

We enter into out-license and collaboration agreements which are within the scope of ASC 606, under which we license certain rights to our product candidates to third parties. The terms of these arrangements typically include payment to us of one or more of the following: non-refundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services we provide through our contract manufacturers; and royalties on net sales of licensed products. Each of these payments may result in license, collaboration and other revenue, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

For elements of our collaboration agreements that are accounted for pursuant to ASC 606, we must develop assumptions that require judgment to determine whether the individual promises should be accounted for as separate performance obligations or as a combined performance obligation, and to determine the stand-alone selling price for each performance obligation identified in the contract. We use key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates, and probabilities of technical and regulatory success. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in an out-license and collaboration arrangement, we recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. With regard to the Otsuka collaboration agreements, we recognize revenue related to amounts allocated to the identified performance obligation on a proportional performance basis as the underlying services are performed.

The preceding estimates and judgments materially affect our recognition of collaboration revenues. Changes in our estimates of forecasted development costs could impact proportional performance percentages and could have a material effect on collaboration revenue recorded in the period in which we determine that change occurs.

Inventory

We value our inventories at the lower-of-cost or net realizable value. We determine the cost of our inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. We classify inventory costs as long-term, in other assets in our consolidated balance sheets, when we expect to utilize the inventory beyond our normal operating cycle.

We perform an assessment of the recoverability of capitalized inventory during each reporting period, and write down any excess and obsolete inventory to our net realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded as a component of cost of product sales in the consolidated statements of operations and comprehensive loss. The determination of whether inventory costs will be realizable requires the use of estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required. Additionally, our product is subject to strict quality control and monitoring that we perform throughout the manufacturing process. In the event that certain batches or units of product do not meet quality specifications, we will record a charge to cost of product sales, to write-down any unmarketable inventory to its estimated net realizable value. In all cases, product inventory is carried at the lower of cost or its estimated net realizable value.

Excess Purchase Commitment Liability

We identified executory contracts in the commercial supply agreements between Keryx and its contract manufacturers for Auryxia, which include future firm purchase commitments. These executory contracts were deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast and as such, we recorded a liability in purchase accounting. We re-evaluate the excess purchase commitments each reporting period to assess whether any adjustments to the excess purchase commitment liability are necessary. This evaluation includes reviewing the contractual minimums, expiration and utilization assumptions, and sales forecasts. Inventory receipts that have been previously identified as excess are recorded as a reduction to the excess purchase commitment liability.

Liability Related to Sale of Future Royalties

We treat the liability related to sale of future royalties as a debt financing, amortized under the effective interest rate method over the estimated life of the related expected royalty stream. The liability related to sale of future royalties and the debt amortization are based on our current estimates of future royalties expected to be paid over the life of the arrangement. We will

periodically assess the expected royalty payments. To the extent our estimates of future royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, we will adjust the effective interest rate and recognize related non-cash interest expense on a prospective basis. Changes in our estimates of future royalty payments could have a material effect on the liability related to sale of future royalties balance recorded in the period in which we determine that change occurs.

Intangible Assets

We maintain a definite-lived intangible asset related to developed product rights for Auryxia, which was acquired on December 12, 2018 as part of the Merger.

Intangible assets are initially recorded at fair value and stated net of accumulated amortization and impairments. We amortize our intangible assets that have finite lives using either the straight-line method, or if reliably determinable, based on the pattern in which the economic benefit of the asset is expected to be utilized. Amortization for our intangible asset is recorded over its remaining estimated useful life, which as of December 31, 2021 is estimated to be six years.

We review intangible assets subject to amortization to determine if any adverse conditions exist or a change in circumstances has occurred that would indicate impairment or a change in the remaining useful life. If an impairment indicator exists, we perform a recoverability test by comparing the sum of the estimated undiscounted cash flows of the intangible asset group to its carrying value on the consolidated balance sheet. If the carrying value of the intangible asset group exceeds the undiscounted cash flows used in the recoverability test, we will write the carrying value of the intangible asset group down to the fair value in the period identified. We calculate the fair value of the intangible asset group as the present value of estimated future cash flows expected to be generated from the intangible asset group using a risk-adjusted discount rate. In determining estimated future cash flows associated with the intangible asset group, we use market participant assumptions pursuant to ASC Topic 820, *Fair Value Measurements and Disclosures* (ASC 820). During the second quarter of 2020, we identified indicators of impairment related to the developed product rights for Auryxia and recorded an impairment charge of $115.5 million (see Note 9 contained in this Annual Report on Form 10-K for additional information).

Income Taxes

Income taxes are recorded in accordance with FASB Topic 740, *Income Taxes*, or ASC 740, which provides for deferred taxes using an asset and liability approach. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. All deferred taxes as of December 31, 2021 and 2020 are classified as noncurrent within the income tax provision (see Note 14 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data).

Recent Accounting Pronouncements

For additional discussion of recent accounting pronouncements, please refer to *New Accounting Pronouncements – Recently Adopted* and *New Accounting Pronouncements – Not Yet Adopted* included within Note 2 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2021 and 2020, we had cash and cash equivalents and available for sale securities of $149.8 million and $268.7 million, respectively, consisting primarily of money market mutual funds consisting of U.S. government debt securities, certificates of deposit and corporate debt securities. Interest rate sensitivity is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our investments are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

In addition, we are exposed to market risk related to exchange rates. A substantial portion of our revenues for the year ended December 31, 2021 was received in U.S. dollars, including revenues we receive from royalty payments converted to U.S. dollars based on the net sales of Riona® and Vafseo™, in Japanese yen. Our exchange rate risk arises from such foreign currency net sales. As a result, we are exposed to movements in the exchange rates of the Japanese yen against the U.S. dollar.

For the royalty payments we received based on net sales of Riona and Vafseo in Japan during the year ended December 31, 2021, a 5.0% appreciation or depreciation of the Japanese yen against the U.S. dollar would have increased or decreased, respectively, our revenues in the year ended December 31, 2021 by approximately $0.3 million.

We have generally accepted the exposure to exchange rate movements without using derivative financial instruments to manage this foreign currency risk.

Item 8. Financial Statements and Supplementary Data

Akebia Therapeutics, Inc.

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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Akebia Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Akebia Therapeutics, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 1, 2022 expressed an adverse opinion thereon.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and managements' plans regarding these matters are described in Note 1. The consolidated financial statements do not include any adjustments that might results from the outcome of uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Valuation of Excess Purchase Commitment Liability

Description of the Matter

At December 31, 2021, the Company's liability for excess purchase commitments related to executory contracts for Auryxia was $76.7 million. As described in Note 16, the Company records a liability for its future firm purchase commitments that exceed the Company's current forecasts. The Company re-evaluates its excess purchase commitments each reporting period to assess whether any adjustments to its excess purchase commitments liability are necessary. This evaluation includes reviewing the contractual minimums, expiration and utilization assumptions, and sales forecasts. Inventory receipts that have been previously identified as excess are recorded as a reduction to the excess purchase commitment liability. The Company's quarterly evaluations of for Auryxia sales forecasts, along with an amendment to a supplier agreement, resulted in the Company recording total charges to cost of sales to increase its liability for excess purchase commitments of $33.4 million during the year ended December 31, 2021. These charges are offset by inventory receipts that had been previously identified as excess totaling $12.5 million.

How We Addressed the Matter in Our Audit

Auditing the Company's evaluation of its excess purchase commitment liability involved complex judgment due to the significant management judgments required to estimate the value of the total excess commitment. The Company's model for estimating the liability involves significant assumptions, including projected sales volumes, which is sensitive to and affected by economic, industry and company-specific qualitative factors.

We obtained an understanding, evaluated the design, and tested controls over the Company's evaluation of its excess purchase commitment liability. This included controls over the model, significant assumptions, and completeness and accuracy of the data used in the evaluation.

To test the Company's evaluation of its excess purchase commitment liability, we performed audit procedures that included, among others, testing the significant inputs and assumptions discussed above, including the completeness and accuracy of the underlying data used by the Company in its analyses. We compared the significant assumptions used by management to current industry and economic trends, historical financial results, contractual obligations, and other relevant factors. We also performed a sensitivity analysis of the significant assumptions to evaluate the change in the liability that would result from changes in underlying assumptions.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.

Boston, Massachusetts
March 1, 2022

AKEBIA THERAPEUTICS, INC.

Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 149,800	$ 228,698
Available for sale securities	—	39,992
Inventory	38,195	61,017
Accounts receivable, net	50,875	26,853
Prepaid expenses and other current assets	33,140	14,877
Total current assets	272,010	371,437
Property and equipment, net	6,754	8,622
Operating lease assets	33,852	26,876
Goodwill	55,053	55,053
Other intangible assets, net	108,127	144,170
Other assets	49,754	37,981
Total assets	$ 525,550	$ 644,139
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 33,588	$ 41,308
Accrued expenses and other current liabilities	104,456	130,624
Short-term deferred revenue	20,906	15,214
Current portion of long-term debt	97,543	—
Total current liabilities	256,493	187,146
Deferred revenue, net of current portion	21,474	25,345
Operating lease liabilities, net of current portion	33,703	24,621
Derivative liability	1,820	2,420
Long-term debt, net	—	96,378
Liability related to sale of future royalties, net	53,079	—
Other non-current liabilities	82,525	60,611
Total liabilities	449,094	396,521
Commitments and contingencies (Note 16)		
Stockholders' equity:		
Preferred stock $0.00001 par value, 25,000,000 shares authorized at December 31, 2021 and 2020; 0 shares issued and outstanding at December 31, 2021 and 2020	—	—
Common stock: $0.00001 par value; 350,000,000 shares authorized at December 31, 2021 and 2020, respectively; 177,000,963 and 148,074,085 shares issued and outstanding at December 31, 2021 and 2020, respectively	1	1
Additional paid-in capital	1,536,800	1,425,115
Accumulated other comprehensive gain	6	13
Accumulated deficit	(1,460,351)	(1,177,511)
Total stockholders' equity	76,456	247,618
Total liabilities and stockholders' equity	$ 525,550	$ 644,139

See accompanying notes to consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

	Year Ended December 31,		
	2021	2020	2019
Revenues:			
Product revenue, net	$ 142,216	$ 128,901	$ 111,119
License, collaboration and other revenue	71,362	166,406	223,882
Total revenues	213,578	295,307	335,001
Cost of goods sold:			
Product	117,352	148,866	108,935
Amortization of intangibles	36,042	31,515	36,401
Impairment of intangible asset	—	115,527	—
Total cost of goods sold	153,394	295,908	145,336
Operating expenses:			
Research and development	147,852	218,485	322,969
Selling, general and administrative	174,161	153,947	149,455
License expense	3,489	3,409	3,529
Total operating expenses	325,502	375,841	475,953
Operating loss	(265,318)	(376,442)	(286,288)
Other income (expense):			
Interest income (expense)	(19,936)	(8,871)	792
Other income (expense)	2,414	1,856	(794)
Net loss before income taxes	(282,840)	(383,457)	(286,290)
Benefit from income taxes	—	—	(6,631)
Net loss	$ (282,840)	$ (383,457)	$ (279,659)
Net loss per share - basic and diluted	$ (1.70)	$ (2.77)	$ (2.36)
Weighted-average number of common shares - basic and diluted	165,949,695	138,463,152	118,395,919
Comprehensive loss:			
Net loss	$ (282,840)	$ (383,457)	$ (279,659)
Other comprehensive gain - unrealized gain on securities	(7)	13	261
Total comprehensive loss	$ (282,847)	$ (383,444)	$ (279,398)

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.

Consolidated Statements of Stockholders' Equity

(in thousands, except share and per share data)

	Common Stock					
	Number of Shares	$0.00001 Par Value	Additional Paid-In Capital	Unrealized Gain/Loss	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2018	116,887,518	$ 1	$ 1,150,583	$ (261)	$ (514,395)	$ 635,928
Issuance of common stock, net of issuance costs	4,068,912	—	25,785	—	—	25,785
Proceeds from sale of stock under employee stock purchase plan	87,530	—	383	—	—	383
Exercise of options	362,796	—	560	—	—	560
Retired shares	(55,324)	—	(426)	—	—	(426)
Share-based compensation expense	—	—	11,925	—	—	11,925
Restricted stock unit vesting	323,136	—	—	—	—	—
Unrealized gain	—	—	—	261	—	261
Net loss	—	—	—	—	(279,659)	(279,659)
Balance at December 31, 2019	121,674,568	$ 1	$ 1,188,810	$ —	$ (794,054)	$ 394,757
Issuance of common stock, net of issuance costs	24,133,348	—	209,519	—	—	209,519
Proceeds from sale of stock under employee stock purchase plan	235,658	—	1,100	—	—	1,100
Exercise of options	166,633	—	1,226	—	—	1,226
Share-based compensation expense	—	—	24,460	—	—	24,460
Restricted stock unit vesting	1,863,878	—	—	—	—	—
Unrealized gain	—	—	—	13	—	13
Net loss	—	—	—	—	(383,457)	(383,457)
Balance at December 31, 2020	148,074,085	$ 1	$ 1,425,115	$ 13	$ (1,177,511)	$ 247,618
Issuance of common stock, net of issuance costs	26,352,343	—	88,204	—	—	88,204
Proceeds from sale of stock under employee stock purchase plan	307,193	—	746	—	—	746
Share-based compensation expense	—	—	22,735	—	—	22,735
Restricted stock unit vesting	2,267,342	—	—	—	—	—
Unrealized gain	—	—	—	(7)	—	(7)
Net loss	—	—	—	—	(282,840)	(282,840)
Balance at December 31, 2021	177,000,963	$ 1	$ 1,536,800	$ 6	$ (1,460,351)	$ 76,456

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2021	2020	2019
Operating activities:			
Net loss	(282,840)	(383,457)	(279,659)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,927	2,075	2,245
Amortization of intangibles	36,043	31,515	36,401
Intangible asset impairment charge	—	115,527	—
Non-cash interest expense related to sale of future royalties	9,117	—	—
Non-cash royalty revenue related to sale of future royalties	(821)	—	—
Amortization of premium/discount on investments	(15)	(47)	(819)
Non-cash interest expense	1,165	1,534	786
Non-cash operating lease expense	(1,842)	(2,037)	(2,229)
Write-off of property and equipment	—	—	2,053
Fair value step-up of inventory sold or written off	21,575	68,240	70,444
Write-down of inventory	15,618	20,072	7,112
Change in excess inventory purchase commitments	33,391	25,114	—
Stock-based compensation	22,735	24,460	11,925
Deferred income taxes	—	—	(6,631)
Change in fair value of derivative liability	(600)	286	—
Changes in operating assets and liabilities:			
Accounts receivable	(24,022)	12,011	(22,198)
Inventory	(25,847)	6,163	(29,142)
Prepaid expenses and other current assets	(18,658)	(8,119)	10,541
Operating lease assets	(13,888)	—	—
Other long-term assets	5,674	(2,779)	4,917
Accounts payable	(11,735)	3,678	1,372
Accrued expense	(24,680)	6,356	(27,351)
Operating lease liabilities	15,398	1,411	2,531
Deferred revenue	1,821	(32,391)	(39,739)
Other non-current liabilities	(12,481)	—	—
Net cash used in operating activities	(252,965)	(110,388)	(257,441)
Investing activities:			
Purchase of property and equipment	(59)	(317)	(6,655)
Purchase of available for sale securities	—	(99,932)	—
Proceeds from the maturities of available for sale securities	40,000	60,245	153,110
Proceeds from sales of available for sale securities	—	—	64,721
Net cash provided by (used in) investing activities	39,941	(40,004)	211,176
Financing activities:			
Proceeds from sale of future royalties, net	44,783	—	—
Proceeds from the issuance of common stock, net of issuance costs	88,202	209,419	25,785
Proceeds from the sale of stock under employee stock purchase plan	746	1,100	383
Proceeds from the exercise of stock options	—	1,226	560
Retirement of treasury stock	—	—	(426)
Proceeds from the issuance of debt, net	—	19,975	77,668
Payments on debt	—	—	(15,000)
Net cash provided by financing activities	133,731	231,720	88,970
Increase (decrease) in cash, cash equivalents, and restricted cash	(79,293)	81,328	42,705
Cash, cash equivalents, and restricted cash at beginning of the period	231,132	149,804	107,099
Cash, cash equivalents, and restricted cash at end of the period	$ 151,839	$ 231,132	$ 149,804
Non-cash financing activities			
Unpaid offering costs	$ 2	$ 100	$ —
Cash paid for:			
Interest	9,632	7,843	781

See accompanying notes to consolidated financial statements.

1. Nature of Organization and Operations

Akebia Therapeutics, Inc., referred to as Akebia or the Company, was incorporated in the State of Delaware in 2007. Akebia is a biopharmaceutical company with the purpose of bettering the lives of people living with kidney disease. Akebia's lead investigational product candidate, vadadustat, is an oral therapy for the treatment of anemia due to chronic kidney disease, or CKD. Vadadustat is an oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH inhibitor designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, or HIF, which stimulates erythropoietin, or EPO, production and can lead to red blood cell, or RBC, production and improved oxygen delivery to tissues. The Company submitted a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, for vadadustat in March of 2021 for the treatment of anemia due to CKD in adult patients with CKD on dialysis, or DD-CKD, and adult patients with CKD not on dialysis, or NDD-CKD. The Company's NDA submission was accepted for filing by the FDA in May 2021 and the FDA has indicated that they are not currently planning to hold an Advisory Committee meeting to discuss the application for vadadustat. The FDA also assigned the application standard review and a Prescription Drug User Fee Act, or PDUFA, target action date of March 29, 2022. The Company's collaboration partner, Otsuka Pharmaceutical Co. Ltd., submitted a Marketing Authorization Application, or MAA, for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients to the European Medicines Agency, or EMA, in October 2021. Vadadustat is approved and marketed in Japan as a treatment for anemia due to CKD in both dialysis-dependent and non-dialysis dependent adult patients under the trade name Vafseo™. In addition, the Company has a commercial product, Auryxia® (ferric citrate), which is currently approved by the U.S. Food and Drug Administration, or FDA, and marketed for two indications in the United States, the control of serum phosphorus levels in adult patients with CKD on dialysis, or DD-CKD, and the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or NDD-CKD. Ferric citrate is also approved and marketed in Japan as an oral treatment for the improvement of hyperphosphatemia in patients with DD-CKD and NDD-CKD under the trade name Riona (ferric citrate hydrate).
Since inception, the Company has devoted most of its resources to research and development, including its preclinical and clinical development activities and commercializing Auryxia, and providing general and administrative support for these operations. The Company began recording revenue from the U.S. sales of Auryxia and revenue from sublicensing rights to Auryxia in Japan to the Company's Japanese partners Japan Tobacco, Inc. and its subsidiary Torii Pharmaceutical Co., Ltd., collectively JT and Torii, on December 12, 2018 following the consummation of the Merger with Keryx. Additionally, following regulatory approval of vadadustat in Japan, the Company began recognizing royalty revenues from Mitsubishi Tanabe Pharma Corporation, or MTPC, from the sale of Vafseo in August 2020. In February 2021, the Company entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or the Royalty Agreement, whereby the Company sold its right to receive royalties and sales milestones under its Collaboration Agreement with MTPC, or the MTPC Agreement, subject to certain caps and other terms and conditions (see Note 5 for additional information). The Company has not generated a profit to date and may never generate profits from product sales. Vadadustat and the Company's other potential product candidates are subject to long development cycles, and the Company may be unsuccessful in its efforts to develop, obtain marketing approval for or market vadadustat and its other potential product candidates. If the Company does not successfully commercialize Auryxia, vadadustat or any other potential product candidate, it may be unable to achieve profitability.

Going Concern

As of December 31, 2021, the Company had cash and cash equivalents of approximately $149.8 million. The Company expects its cash resources to fund its current operating plan for at least twelve months from the date of this filing. However, the potential timely regulatory approval of vadadustat and the receipt of associated regulatory milestones is an important source of funding of our cash runway, which is outside of the Company's control. There can be no assurance that the current operating plan, including with respect to vadadustat, if approved, will be achieved in the time frame anticipated by the Company, or that its cash resources will fund the Company's operating plan for the period anticipated by the Company or that additional funding will be available on terms acceptable to the Company, or at all.

In addition, on February 18, 2022, the Company and BioPharma Credit PLC, or the Collateral Agent, BPCR Limited Partnership, as a Lender, and BioPharma Credit Investments V (Master) LP. as a Lender, entered into the First Amendment and Waiver, or the First Amendment and Waiver, which amends and waives certain provisions of the Loan Agreement, dated November 11, 2019 (see Note 18). Pursuant to the Loan Agreement, as amended, the Company's filings of Form 10-Q for fiscal quarters ending June 30, 2022 and September 30, 2022, and its future Annual Reports on Form 10-K, must not be subject to any qualification as to going concern. If the Company does not satisfy the covenant as to going concern in any of these filings, the Company will be in default under the Loan Agreement. If an event of default occurs and is continuing under the Loan

Agreement, the Collateral Agent is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement, which the Company may not have the available cash resources to repay at such time.

The Company's management completed its going concern assessment in accordance with ASC 205-40, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASC 205-40. Pursuant to the requirements of ASC 205-40, the Company's management must evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued.

When substantial doubt exists under this methodology, the Company's management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of the Company's plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued.

The Company believes that its cash resources will be sufficient to allow the Company to fund its current operating plan through at least the next twelve months from the filing of the Company's 2021 Annual Report on Form 10-K. However, as certain elements of the Company's operating plan are outside of the Company's control, including the potential timely regulatory approval of vadadustat and the receipt of associated regulatory milestones, they cannot be considered probable under ASC 205-40. There also is uncertainty as to whether or not the Company will meet our quarterly and annual debt covenants.

These conditions raise substantial doubt regarding the Company's ability to continue as a going concern for a period of one year after the date the financial statements are issued. The Company will require additional capital to fund its operating plan beyond the next twelve months, including pursuing development and commercial activities related to Auryxia and vadadustat, if approved, or any additional products and product candidates, including those that may be in-licensed or acquired. The Company expects to finance future cash needs through product revenue Management's plans to alleviate the conditions that raise substantial doubt include raising additional funding through product revenue, earning milestone payments pursuant to the Company's collaboration agreements, public or private equity or debt transactions, payments from its collaborators, strategic transactions, or a combination of these approaches. However, adequate additional financing may not be available to the Company on acceptable terms, or at all. If the Company is unable to raise capital in sufficient amounts when needed or on attractive terms, it may not be able to pursue development and commercial activities related to Auryxia and vadadustat or any additional products and product candidates, including those that may be in-licensed or acquired. for the Company to continue as a going concern for a period of twelve months from the date the financial statements are issued. The Company has concluded the likelihood that its plan to obtain sufficient funding from one or more of these sources will be successful, while reasonably possible, is less than probable. Accordingly, the Company has concluded that substantial doubt exists about the Company's ability to continue as a going concern for a period of at least twelve months from the date of issuance of these financial statements.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities, other than obligations under the Loan Agreement classified as current, that might result from the outcome of the uncertainties described above.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. These consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification, or ASC, and Accounting Standards Update, or ASU, of the Financial Accounting Standards Board, or FASB.

New Accounting Pronouncements – Recently Adopted

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes.* This standard became effective for the Company on January 1, 2021. ASU 2019-12 requires certain amendments to be applied using a modified retrospective approach, which requires a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year of adoption, while other amendments should be applied on a prospective basis. The adoption of this standard did not have a material impact on the Company's consolidated financial statements and related disclosures.

New Accounting Pronouncements – Not Yet Adopted

In March 2020, the FASB issued ASU 2020-04, *Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting*. The amendments provide optional guidance for a limited time to ease the potential burden in accounting for reference rate reform. The new guidance provides optional expedients and exceptions for applying GAAP to contracts, hedging relationships and other transactions affected by reference rate reform if certain criteria are met. The amendments apply only to contracts and hedging relationships that reference LIBOR or another reference rate expected to be discontinued due to reference rate reform. These amendments are effective immediately and may be applied prospectively to contract modifications made and hedging relationships entered into or evaluated on or before December 31, 2022. The Company is currently evaluating its contracts and the optional expedients provided by the new standard.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing novel therapeutics for people with kidney disease.

Derivative Financial Instruments

The Company accounts for warrants and other derivative financial instruments as either equity or liabilities in accordance with ASC Topic 815, *Derivatives and Hedging*, or ASC 815, based upon the characteristics and provisions of each instrument. Warrants classified as equity are recorded at fair value as of the date of issuance on the Company's consolidated balance sheets and no further adjustments to their valuation are made. Warrants classified as derivative liabilities and other derivative financial instruments that require separate accounting as liabilities are recorded on the Company's consolidated balance sheets at their fair value on the date of issuance and will be revalued on each subsequent balance sheet date until such instruments are exercised or expire, with any changes in the fair value between reporting periods recorded as other income or expense. The warrant issued by the Company in connection with the Janssen Pharmaceutica NV Research and License Agreement, the Janssen Agreement, is classified as equity in the Company's consolidated balance sheet at December 31, 2021 (see Note 12). The derivative liability recorded in connection with the Company's Loan Agreement with Pharmakon is classified as a liability in the Company's consolidated balance sheet (see Note 11).

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results may differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes, and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: prepaid and accrued research and development expense, operating lease assets and liabilities, derivative liabilities, other non-current liabilities, including the excess purchase commitment liability, stock-based compensation expense, product and collaboration revenues including various rebates and reserves related to product sales, non-cash interest expense on the liability related to sale of future royalties, inventories, income taxes, intangible assets and goodwill. The Company has made estimates of the impact of COVID-19 within the consolidated financial statements and there may be changes to those estimates in future periods including changes to sales, payer mix, reserves and allowances, intangible assets and goodwill.

Although the Company regularly assesses these estimates, actual results could differ materially from these estimates. Changes in estimates are recorded in the period they become known. The Company bases its estimates on historical experience and various other assumptions that it believes to be reasonable under the circumstances.

Credit Losses

Available for sale debt securities. Management determines the appropriate classification of securities at the time of purchase and reevaluates such designation as of each balance sheet date. The Company classifies all securities as available for sale and includes them in current assets as they are intended to fund current operations. The Company's investment portfolio at any point in time contains investments in money market mutual funds, U.S. government debt securities, certificates of deposit and corporate debt securities. The Company segments its portfolio based on the underlying risk profiles of the securities and have a zero loss expectation for money market mutual funds, U.S. government debt securities and certificates of deposit. The Company regularly reviews the securities in an unrealized loss position and evaluates the current expected credit loss by considering factors such as historical experience, market data, issuer-specific factors, and current economic conditions. Factors considered also include whether a decline in fair value below the amortized cost basis is due to credit-related factors or noncredit-related factors, the financial condition and near-term prospects of the issuer, and the Company's intent and ability to hold the investment to allow for an anticipated recovery in fair value. Any unrealized loss that is not credit related is recognized in other comprehensive (loss) income in the consolidated statements of operations. A credit-related unrealized loss is recognized as an allowance on the consolidated balance sheets with a corresponding adjustment to earnings in the consolidated statements of operations.

Cash, Cash Equivalents, and Restricted Cash

Cash and cash equivalents consist of all cash on hand, deposits and funds invested in available for sale securities with original maturities of three months or less at the time of purchase. Cash equivalents are reported at fair value. At December 31, 2021, the Company’s cash is primarily in money market funds. The Company may maintain balances with its banks in excess of federally insured limits.

Restricted cash represents amounts required for security deposits under the Company’s office and lab space lease agreements. Restricted cash is included in “prepaid expenses and other current assets” and “other assets” in the consolidated balance sheets.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported in the consolidated balance sheet that sum to the total of the amounts reported in the consolidated statement of cash flows (in thousands):

	December 31, 2021	December 31, 2020	December 31, 2019
Cash and cash equivalents	$ 149,800	$ 228,698	$ 147,449
Prepaid expenses and other current assets	—	395	263
Other assets	2,039	2,039	2,092
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$ 151,839	$ 231,132	$ 149,804

Investments

Management determines the appropriate classification of securities at the time of purchase and reevaluates such designation as of each balance sheet date. Currently, the Company classifies all securities as available for sale which are included in current assets as they are intended to fund current operations. The Company carries available for sale securities at fair value. The Company conducts periodic reviews to identify and evaluate each investment that has an unrealized loss, in accordance with the meaning of other-than-temporary impairment and its application to certain investments. When assessing whether a decline in the fair value of a security is other-than-temporary, the Company considers the fair market value of the security, the duration of the security’s decline, and prospects for the underlying business. Based on these considerations, the Company did not identify any other-than-temporary unrealized losses at December 31, 2021. Unrealized losses on available for sale securities that are determined to be temporary, and not related to credit loss, are recorded in accumulated other comprehensive loss, a component of stockholders’ equity. The amortized cost of debt securities in this category reflects amortization of premiums and accretion of discounts to maturity computed under the effective interest method. The Company includes this amortization in the caption “Interest income, net” within the consolidated statements of operations and comprehensive loss. The Company also includes in net investment income, realized gains and losses and declines in value determined to be other than temporary. The Company

bases the cost of securities sold upon the specific identification method and includes interest and dividends on securities in interest income.

Accounts Receivable

The Company's accounts receivable represent amounts due to the Company from product sales (see Note 3) and from its collaboration agreements with MTPC and Otsuka (see Note 4). Reimbursable costs that have not been invoiced as of the balance sheet date are recorded as unbilled accounts receivable. Accounts receivable arising from product sales primarily represent amounts due from wholesale distributors as well as certain specialty pharmacy providers, or collectively, Customers. The Company deducts trade allowances for prompt payment, among other discounts, from its accounts receivable based on its experience that the Company's Customers will earn these discounts and fees.

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed as well as historical payment patterns and existing economic factors. The Company believes that credit risks associated with its customers and collaboration partners are not significant. The Company did not have a material allowance for doubtful accounts as of December 31, 2021 and 2020.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Cash, cash equivalents, investments, and accounts receivable are the only financial instruments that potentially subject the Company to concentrations of credit risk. The Company maintains its cash, cash equivalents, and investments with high quality, accredited financial institutions and, accordingly, such funds are subject to minimal credit risk. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Accounts receivable represent amounts due from the Company's customers and collaboration partners. As part of its credit management policy, the Company performs ongoing credit evaluations of its Customers and generally does not require collateral from any customer. The Company also monitors economic conditions of its collaboration partners to identify facts or circumstances that may indicate that any of its accounts receivable are at risk of collection.

Gross revenues and accounts receivable from each of the Company's Customers or collaboration partners who individually accounted for 10% or more of total gross revenues and/or 10% or more of total gross accounts receivable consisted of the following:

	Percent of Total Gross Revenues		
	Years Ended December 31,		
	2021	2020	2019
Fresenius Medical Care Rx	33 %	29 %	21 %
AmerisourceBergen Drug Corporation	16 %	12 %	10 %
Otsuka Pharmaceutical Co. Ltd.	14 %	29 %	45 %
McKesson Corporation	13 %	11 %	— %
Cardinal Health, Inc.	11 %	— %	— %

	Percent of Gross Accounts Receivable	
	As of December 31,	
	2021	2020
Otsuka Pharmaceutical Co. Ltd.	22 %	— %
MTPC	20 %	— %
Fresenius Medical Care Rx	16 %	19 %
AmerisourceBergen Drug Corporation	15 %	29 %
Cardinal Health, Inc.	10 %	14 %
McKesson Corporation	— %	12 %

Property and Equipment

Property and equipment is stated at cost, less accumulated depreciation. Assets under capital lease are included in property and equipment. Property and equipment is depreciated using the straight-line method over the estimated useful lives of the assets, generally three years to seven years. Such costs are periodically reviewed for recoverability when impairment indicators are present. Such indicators include, among other factors, unused capacity, market value declines and technological obsolescence. Recorded values of asset groups of equipment that are not expected to be recovered through undiscounted future net cash flows are written down to current fair value, which generally is determined from estimated discounted future net cash flows (assets held for use) or net realizable value (assets held for sale).

The following is the summary of property and equipment and related accumulated depreciation as of December 31, 2021 and 2020.

	Useful Life	December 31, 2021	December 31, 2020
		(in thousands)	
Computer equipment and software	3	$ 1,010	$ 1,010
Furniture and fixtures	5 - 7	2,086	2,086
Equipment	7	2,750	2,692
Leasehold improvements	Shorter of the useful life or remaining lease term	8,573	8,573
		14,419	14,361
Less accumulated depreciation		(7,665)	(5,739)
Net property and equipment		$ 6,754	$ 8,622

Depreciation expense was approximately $1.9 million, $2.1 million and $2.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

Leases

In February 2016, the FASB issued ASU 2016-02, *Leases* (Topic 842), which supersedes the existing guidance for lease accounting, Leases (Topic 840). ASU 2016-02 requires entities to recognize right-of-use assets and lease liabilities for leases with lease terms of more than 12 months on their balance sheets and provide enhanced disclosures. In 2018, the FASB issued additional ASUs related to Topic 842, or ASC 842, that clarified various aspects of the new lease guidance, including how to record certain transition adjustments, as well as other improvements and practical expedients.

The Company made an accounting policy election not to recognize leases with an initial term of 12 months or less within its consolidated balance sheets and to recognize those lease payments on a straight-line basis in its consolidated statements of operations. The Company also made the accounting policy election not to separate the non-lease components from the lease components for its building leases and, rather, account for each non-lease component and lease component as a single component.

The Company determines if an arrangement is a lease at inception. An arrangement is determined to contain a lease if the contract conveys the right to control the use of an identified property, plant, or equipment for a period of time in exchange for consideration. If the Company can benefit from the various underlying assets of a lease on their own or together with other resources that are readily available, or if the various underlying assets are neither highly dependent on nor highly interrelated with other underlying assets in the arrangement, they are considered to be a separate lease component. In the event multiple underlying assets are identified, the lease consideration is allocated to the various components based on each of the component's relative fair value.

Operating lease assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent its obligation to make lease payments arising from the leasing arrangement. Operating lease assets and operating lease liabilities are recognized at the commencement date based on the present value of lease payments over the lease term. The Company uses the implicit rate when readily determinable and uses an estimate of its incremental borrowing rate when the implicit rate is not readily determinable based upon the available information at the commencement date of lease inception. The incremental borrowing rate is determined using a credit rating scoring model to estimate the Company's credit rating, adjusted for collateralization. The calculation of the operating lease assets includes any lease payments made and excludes any lease incentives. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option.

The Company's operating leases are reflected in prepaid expenses and other current assets, operating lease assets, accrued expenses and operating lease liabilities, net of current portion in its consolidated balance sheets. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

Inventory

The Company values its inventories at the lower-of-cost or net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. The Company classifies its inventory costs as long-term, in other assets in its consolidated balance sheets, when it expects to utilize the inventory beyond their normal operating cycle.

Prior to the regulatory approval of a product candidate, the Company incurs expenses for the manufacture of material that could potentially be available to support the commercial launch of its products upon approval. Until the first reporting period when regulatory approval has been received or is otherwise considered probable and the future economic benefit is expected to be realized, the Company records all such costs as research and development expense. Inventory used in clinical trials is also expensed as research and development expense, when selected for such use. Inventory that can be used in either the production of clinical or commercial products is expensed as research and development costs when identified for use in a clinical manufacturing campaign.

The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and writes down any excess and obsolete inventory to its net realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded as a component of cost of product sales in the consolidated statements of operations and comprehensive loss. The determination of whether inventory costs will be realizable requires the use of estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required. Additionally, the Company's product is subject to strict quality control and monitoring that it performs throughout the manufacturing process. In the event that certain batches or units of product do not meet quality specifications, the Company will record a charge to cost of product sales, to write-down any unmarketable inventory to its estimated net realizable value. In all cases, product inventory is carried at the lower of cost or its estimated net realizable value.

Debt

The Company performs an assessment of all embedded features of a debt instrument to determine if (1) such features should be bifurcated and separately accounted for, and (2) if bifurcation requirements are met, whether such features should be classified and accounted for as equity or liability instruments. If the embedded feature meets the requirements to be bifurcated and accounted for as a liability, the fair value of the embedded feature is measured initially, included as a liability on the consolidated balance sheet, and re-measured to fair value at each reporting period. Any changes in fair value are recorded in the consolidated statement of operations. The Company monitors, on an ongoing basis, whether events or circumstances could give rise to a change in the classification of embedded features.

Liability Related to Sale of Future Royalties

The Company treats the liability related to sale of future royalties (see Note 5) as a debt financing, amortized under the effective interest rate method over the estimated life of the related expected royalty stream. The liability related to sale of future royalties and the debt amortization are based on the Company's current estimates of future royalties expected to be paid over the life of the arrangement. The Company will periodically assess the expected royalty payments. To the extent the Company's estimates of future royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, the Company will adjust the effective interest rate and recognize related non-cash interest expense on a prospective basis. Non-cash royalty revenue is reflected as royalty revenue within license, collaboration and other revenue, and non-cash amortization of debt is reflected as interest expense in the unaudited condensed consolidated statements of operations and comprehensive loss.

Excess Purchase Commitment Liability

The Company identified executory contracts in the commercial supply agreements between Keryx and its contract manufacturers for Auryxia, which include future firm purchase commitments. These executory contracts were deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast and as such, the Company recorded a liability in purchase accounting. The Company re-evaluates the excess purchase commitments each reporting period to assess whether any adjustments to the excess purchase commitment liability are necessary. This evaluation

includes reviewing the contractual minimums, expiration and utilization assumptions, and sales forecasts. Inventory receipts that have been previously identified as excess are recorded as a reduction to the excess purchase commitment liability.

Revenue Recognition

The Company generates revenues primarily from sales of Auryxia, see Note 3, and from its collaborations with MTPC and Otsuka, see Note 4. The Company recognizes revenue in accordance with ASC 606, which applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, it performs the following five steps:

(i) identify the contract(s) with a customer;
(ii) identify the performance obligations in the contract;
(iii) determine the transaction price;
(iv) allocate the transaction price to the performance obligations in the contract; and
(v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company does not include a financing component to its estimated transaction price at contract inception unless it estimates that certain performance obligations will not be satisfied within one year. Additionally, the Company recognizes the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that the Company otherwise would have recognized is one year or less.

Product Revenue, Net

The Company sells Auryxia in the United States, or U.S., primarily to wholesale distributors as well as certain specialty pharmacy providers, collectively, Customers. These Customers resell the Company's product to health care providers and patients. In addition to distribution agreements with Customers, the Company enters into arrangements with health care providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks, and discounts with respect to the purchase of the Company's product.

The Company recognizes revenue on product sales when the Customer obtains control of the Company's product, which occurs at a point in time, typically upon delivery to the Customer. The Company expenses incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that it would have recognized is one year or less.

Reserves for Variable Consideration

Revenue from product sales is recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and which result from discounts, returns, chargebacks, rebates, co-pay assistance and other allowances that are offered within contracts between the Company and its Customers, health care providers, payors and other indirect customers relating to the Company's sales of its products. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount will be credited to the Customer) or as a current liability (if the amount is payable to a Customer or a party other than a Customer). When appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as the Company's historical experience, current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the respective underlying contracts.

The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's

estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances: The Company generally provides Customers with discounts that include incentive fees that are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, the Company compensates (through trade discounts and allowances) its Customers for sales order management, data, and distribution services. However, the Company has determined such services received to date are not distinct from the Company's sale of products to the Customer and, therefore, these payments have been recorded as a reduction of revenue within the consolidated statement of operations and comprehensive loss through December 31, 2021. The Company records a corresponding reduction to accounts receivable (if the trade discount and/or allowance will be credited to the Customer) or an increase to accrued expense (if the trade discount and/or allowance is payable to a Customer) on the consolidated balance sheets.

Product Returns: Consistent with industry practice, the Company generally offers Customers a limited right of return which allows for the product to be returned when the product expiry is within an allowable window, when the quantity delivered is different than quantity ordered, the product is damaged in transit prior to receipt by the customer, or is subject to a recall. This right of return generally lapses once the product is provided to a patient. The Company estimates the amount of its product sales that may be returned for credit by its Customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized. The Company currently estimates product return reserve using available industry data and its own historical sales information, including its visibility into the inventory remaining in the distribution channel.

Provider Chargebacks and Discounts: Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by Customers, and the Company generally issues credits for such amounts within a few weeks of the Customer's resale of the product. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel at each reporting period end that the Company expects will be sold to qualified healthcare providers, and chargebacks that Customers have claimed but for which the Company has not yet issued a credit.

Commercial and Medicare Part D Rebates: The Company contracts with various commercial payor organizations, primarily health insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of its products. The Company estimates the rebates for commercial and Medicare Part D payors based upon (i) its contracts with the payors and (ii) information obtained from its Customers and other third parties regarding the payor mix for Auryxia. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Other Government Rebates: The Company is subject to discount obligations under state Medicaid programs and other government programs. The Company estimates its Medicaid and other government programs rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

Other Incentives: Other incentives that the Company offers include voluntary patient assistance programs such as the Company's co-pay assistance program, which are intended to provide financial assistance to qualified commercially insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on actual claims processed during a given period, as well as historical utilization data to estimate the amount the Company expects to receive associated with product that has been recognized as revenue, but remains in in the distribution channel at the end of each reporting period.

Collaboration Revenues

The Company enters into out-license and collaboration agreements which are within the scope of ASC 606, under which it licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services the Company provides through its contract manufacturers; and royalties on net sales of licensed products. Each of these payments may result in license, collaboration and other revenue, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements, the Company implements the five-step model noted above. As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine whether the individual promises should be accounted for as separate performance obligations or as a combined performance obligation, and to determine the stand-alone selling price for each performance obligation identified in the contract. A deliverable represents a separate performance obligation if both of the following criteria are met: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer, and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates, and probabilities of technical and regulatory success. With regard to the MTPC and Otsuka collaboration agreements, the Company recognizes revenue related to amounts allocated to the identified performance obligation on a proportional performance basis as the underlying services are performed.

Licenses of Intellectual Property

If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in an out-license and collaboration arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments

At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to assess the milestone as probable of being achieved. There is considerable judgment involved in determining whether a milestone is probable of being reached at each specific reporting period. Milestone payments that are not within the control of the Company or the customer, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenues as, or when, the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue in the period of adjustment.

Manufacturing Supply Services

Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. The Company assesses if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations. If the Company is entitled to additional payments when the licensee exercises these options, any additional payments are recorded in license, collaboration and other revenues when the licensee obtains control of the goods, which is upon delivery.

Royalties

The Company will recognize sales-based royalties, including milestone payments based on the level of sales, at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has

been satisfied (or partially satisfied). The Company receives royalty payments from JT and Torii, based on net sales of Riona, and MTPC based on net sales of Vafseo in Japan.

Collaborative Arrangements

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with ASC Topic 808, *Collaborative Arrangements* (ASC 808). Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities are recorded as collaborative arrangements. The Company considers the guidance in ASC 606-10-15, *Revenue from Contracts with Customers – Scope and Scope Exceptions*, in determining the appropriate treatment for the transactions between the Company and its collaborative partners and the transactions between the Company and third parties. Generally, the classification of transactions under the collaborative arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants. Therefore, the Company recognizes its allocation of the shared costs incurred with respect to the jointly conducted medical affairs and commercialization and non-promotional activities under the Otsuka U.S. Agreement, as defined below in Note 4, as a component of the related expense in the period incurred. To the extent product revenue is generated from the collaboration, the Company recognizes its share of the net sales on a gross basis if the Company is deemed to be the principal in the transactions with customers, or on a net basis if the Company is instead deemed to be the agent in the transactions with customers, consistent with the guidance in ASC 606.

Business Combinations and Asset Acquisitions

The purchase price allocation for business combinations requires extensive use of accounting estimates and judgments to allocate the purchase price to the identifiable tangible and intangible assets acquired and liabilities assumed based on their respective fair values. Under ASU No. 2017-01, “Business Combinations (Topic 805): Clarifying the Definition of a Business (“2017-01”), the Company first determines whether substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or a group of similar identifiable assets. If this threshold is met, the single asset or group of assets, as applicable, is not a business.

The Company accounts for acquired businesses using the acquisition method of accounting, under which the total purchase price of an acquisition is allocated to the net tangible and identifiable intangible assets acquired and liabilities assumed based on their estimated fair values as of the acquisition date. In determining fair value, the Company uses market participant assumptions pursuant to ASC Topic 820, *Fair Value Measurements and Disclosures* (ASC 820). Acquisition-related costs are expensed as incurred. Any excess of the consideration transferred over the estimated fair values of the identifiable net assets acquired is recorded as goodwill.

The purchase price allocations are initially prepared on a preliminary basis and are subject to change as additional information becomes available concerning the fair value and tax basis of the assets acquired and liabilities assumed. Any adjustments to the purchase price allocations are made as soon as practicable but no later than one year from the acquisition date.

Acquired inventory is recorded at its fair value, which may require a step-up adjustment to recognize the inventory at its expected net realizable value. The inventory step-up is recorded to cost of product sales in the Company's consolidated statements of operations when related inventory is sold, and the Company records step-up costs associated with clinical trial material as research and development expense.

Intangible Assets

The Company maintains a definite-lived intangible asset related to developed product rights for Auryxia, which was acquired on December 12, 2018 as part of the Merger.

Intangible assets are initially recorded at fair value and stated net of accumulated amortization and impairments. The Company amortizes its intangible assets that have finite lives using either the straight-line method, or if reliably determinable, based on the pattern in which the economic benefit of the asset is expected to be utilized. Amortization for the Company’s intangible asset is recorded over its remaining estimated useful life, which as of December 31, 2021 is estimated to be six years.

The Company reviews intangible assets subject to amortization to determine if any adverse conditions exist or a change in circumstances has occurred that would indicate impairment or a change in the remaining useful life. If an impairment indicator exists, the Company performs a recoverability test by comparing the sum of the estimated undiscounted cash flows of the intangible asset group to its carrying value on the consolidated balance sheet. If the carrying value of the intangible asset group exceeds the undiscounted cash flows used in the recoverability test, the Company will write the carrying value of the intangible

asset group down to the fair value in the period identified. The Company calculates the fair value of the intangible asset group as the present value of estimated future cash flows expected to be generated from the intangible asset group using a risk-adjusted discount rate. In determining estimated future cash flows associated with its intangible asset group, the Company uses market participant assumptions pursuant to ASC Topic 820, *Fair Value Measurements and Disclosures* (ASC 820). During the second quarter of 2020, the Company identified indicators of impairment related to the developed product rights for Auryxia and recorded an impairment charge of $115.5 million (see Note 9).

Goodwill

The Company allocates any excess purchase price over the fair value of the net tangible and intangible assets acquired in a business combination to goodwill. Goodwill is evaluated for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist.

The Company compares the fair value of its reporting unit to its carrying value. If the carrying value of the net assets assigned to the reporting unit exceeds the fair value of its reporting unit, the Company would record an impairment loss equal to the difference. As described above, the Company operates in one operating segment which the Company considers to be the only reporting unit.

Fair Value of Financial Instruments

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. ASC 820 establishes a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available.

Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments, and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

- Level 1 – Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
- Level 2 – Valuations based on quoted prices for similar assets or liabilities in markets that are not active, or for which all significant inputs are observable, either directly or indirectly.
- Level 3 – Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Items measured at fair value on a recurring basis include available for sale securities and derivative liabilities (see Note 7). The carrying amounts of prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to their short-term maturities.

Items measured at fair value on a nonrecurring basis include property and equipment, intangible assets and goodwill. The Company remeasures the fair value of these assets upon the occurrence of certain events. There were no impairments to assets measured using Level 3 inputs during the year ended December 31, 2021. During the second quarter of 2020, the Company identified indicators of impairment related to the developed product rights for Auryxia, an intangible asset measured using Level 3 inputs, and recorded an impairment charge of $115.5 million (see Note 9). There were no other impairments to assets measured using Level 3 inputs during the year ended December 31, 2020.

The Company's other financial instruments mainly consists of debt (see Note 11). The carrying amount for the Company's Loan Agreement with Pharmakon approximates fair value because the interest rate is variable and reflects current market rates.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses are comprised of costs incurred in providing research and development activities, including salaries and benefits, facilities costs, overhead costs, contract research and development services, and other outside costs. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

External research and development expenses associated with the Company's programs include clinical trial site costs, research compounds and clinical manufacturing costs, costs incurred for consultants and other outside services, such as data management and statistical analysis support, and materials and supplies used in support of the clinical and preclinical programs. Internal costs of the Company's clinical program include salaries, benefits, stock-based compensation, and an allocation of the Company's facility costs. When third-party service providers' billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those third parties, including clinical trial and pharmaceutical development costs, contractual services costs and supply costs, incurred in a given accounting period and record accruals at the end of the period. The Company bases its estimates on its knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the third-party service contract, where applicable.

Advertising Expenses

The costs of advertising are expensed as incurred and included in selling, general and administrative expenses in the consolidated statements of operations and comprehensive loss. For the years ended December 31, 2021, 2020 and 2019, advertising expenses totaled $8.2 million, $5.0 million and $6.0 million, respectively, all related to Auryxia.

Income Taxes

Income taxes are recorded in accordance with FASB Topic 740, *Income Taxes*, or ASC 740, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. All deferred taxes as of December 31, 2021 and 2020 are classified as noncurrent within the income tax provision (see Note 14).

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position, as well as consideration of the available facts and circumstances. As of December 31, 2021 and 2020, the Company does not have any significant uncertain tax positions. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees and non-employees, including grants of stock options, restricted stock, restricted stock units, or RSUs, performance-based restricted stock units, or PSUs, and modifications to existing stock awards, to be recognized in the statements of operations and comprehensive loss based on their fair values. The Company's stock-based awards are comprised of stock options, RSUs and PSUs. The Company estimates the fair value of options granted using the Black-Scholes option pricing model. The Company uses a blend of its stock price and the quoted market price of comparable public companies to determine the fair value of restricted stock awards, common stock awards, and performance-based restricted stock awards.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Prior to 2017, due to the lack of company-specific historical and implied volatility data for trading the Company's stock in the public market, the Company had based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility was calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility was based on the historical volatility of a representative group of companies

with similar characteristics to the Company, including stage of product development and life science industry focus. During 2017, the Company began to estimate its volatility by using a blend of its stock price history for the length of time it has market data for its stock and the historical volatility of similar public companies for the expected term of each grant. The Company is a commercial-stage biopharmaceutical company and the representative group of companies has certain similar characteristics to the Company. The Company believes the group selected has sufficient similar economic and industry characteristics and includes companies that are most representative of the Company. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock, which is similar to the Company's peer group.

The Company's stock-based awards are subject to either service- or performance-based vesting conditions. Compensation expense related to awards to employees and non-employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term, and is adjusted for pre-vesting forfeitures in the period in which the forfeitures occur. Compensation expense related to awards to employees and non-employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

For awards with performance conditions in which the award does not vest unless the performance condition is met, the Company recognizes expense if, and to the extent that, the Company estimates that achievement of the performance condition is probable. If the Company concludes that vesting is probable, it recognizes expense from the date it reaches this conclusion through the estimated vesting date.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted-average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted-average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted net loss per share calculation, preferred stock, stock options, warrants, restricted stock and RSUs are considered to be common stock equivalents, but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented. Diluted net income per share is calculated by dividing the net income by the weighted-average common shares outstanding for the period, including any dilutive effect from outstanding options, warrants, restricted stock and RSUs using the treasury stock method.

3. Product Revenue, Net

To date, the Company's only source of product revenue has been from the U.S. sales of Auryxia. Total net product revenue was $142.2 million, $128.9 million, and $111.1 million for the years ended December 31, 2021, 2020, and 2019, respectively. The following table summarizes activity in each of the product revenue allowance and reserve categories for the years ended December 31, 2019, 2020, and 2021 (in thousands):

	Chargebacks and Discounts	Rebates, Fees and other Deductions	Returns	Total
Balance at December 31, 2018	$ 516	$ 22,861	$ 360	$ 23,737
Provisions related to sales in current year	7,822	110,866	2,008	120,696
Adjustments related to prior year sales	—	1,149	—	$ 1,149
Credits/payments made	(7,600)	(104,324)	(2,115)	$ (114,039)
Balance at December 31, 2019	738	30,552	253	31,543
Current provisions related to sales in current year	10,559	149,472	7,238	167,269
Adjustments related to prior year sales	—	377	—	377
Credits/payments made	(10,495)	(140,489)	(6,842)	(157,826)
Balance at December 31, 2020	$ 802	$ 39,912	$ 649	$ 41,363
Current provisions related to sales in current year	11,759	133,297	5,852	150,908
Adjustments related to prior year sales	(1)	(1,790)	—	(1,791)
Credits/payments made	(11,282)	(144,794)	(6,026)	(162,102)
Balance at December 31, 2021	$ 1,278	$ 26,625	$ 475	$ 28,378

Chargebacks, discounts and returns are recorded as a direct reduction of revenue on the consolidated statement of operations with a corresponding reduction to accounts receivable on the consolidated balance sheets. Rebates, distribution-related fees, and other sales-related deductions are recorded as a reduction in revenue on the consolidated statement of operations with a corresponding increase to accrued liabilities or accounts payable on the consolidated balance sheets.

Accounts receivable, net related to product sales was approximately $24.6 million and $21.9 million as of December 31, 2021 and 2020, respectively.

4. License, Collaboration and Other Significant Agreements

During the years ended December 31, 2021, 2020 and 2019, the Company recognized the following revenues from its license, collaboration and other significant agreements and had the following deferred revenue balances as of December 31, 2021:

	For the Year Ended December 31,		
	2021	2020	2019
License, Collaboration and Other Revenue:		(in thousands)	
MTPC Agreement	$ 12,438	$ 15,405	$ 10,000
Otsuka U.S. Agreement	36,588	93,446	131,314
Otsuka International Agreement	16,449	45,451	75,614
Total Proportional Performance Revenue	$ 65,475	$ 154,302	$ 216,928
JT and Torii	5,814	5,681	5,882
MTPC Other Revenue	73	6,423	1,072
Total License, Collaboration and Other Revenue	$ 71,362	$ 166,406	$ 223,882

	December 31, 2021		
	Short-Term	Long-Term	Total
Deferred Revenue:		(in thousands)	
Otsuka U.S. Agreement	$ 7,970	$ 12,402	$ 20,372
Otsuka International Agreement	5,467	4,393	$ 9,860
MTPC	7,469	—	$ 7,469
Vifor Agreement	—	4,679	$ 4,679
Total	$ 20,906	$ 21,474	$ 42,380

The following table presents changes in the Company’s contract assets and liabilities during the years ended December 31, 2021 and 2020 (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Twelve Months Ended December 31, 2021				
Contract assets:				
Accounts receivable (1)	$ 3,045	$ 64,676	$ (48,627)	$ 19,094
Prepaid expenses and other current assets	$ 1,722	$ 2,592	$ (5)	$ 4,309
Contract liabilities:				
Deferred revenue	$ 40,559	$ 83,491	$ (81,670)	$ 42,380
Accounts payable	$ 7,227	$ 3,171	$ (7,227)	$ 3,171
Accrued expenses and other current liabilities	$ 10,000	$ —	$ (10,000)	$ —
Twelve Months Ended December 31, 2020				
Contract assets:				
Accounts receivable (1)	$ 15,822	$ 161,772	$ (174,549)	$ 3,045
Prepaid expenses and other current assets	$ —	$ 1,722	$ —	$ 1,722
Contract liabilities:				
Deferred revenue	$ 72,950	$ 122,108	$ (154,499)	$ 40,559
Accounts payable	$ —	$ 17,324	$ (10,097)	$ 7,227
Accrued expenses and other current liabilities	$ —	$ 10,615	$ (615)	$ 10,000

(1) Excludes accounts receivable from other services related to clinical and regulatory activities performed by the Company on behalf of MTPC that are not included in the performance obligations identified under the MTPC Agreement as of December 31, 2021 and 2020. Also excludes accounts receivable related to amounts due to the Company from product sales which are included in the accompanying consolidated balance sheets as of December 31, 2021 and 2020.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized the following revenues as a result of changes in the contract asset and contract liability balances in the respective periods (in thousands):

	For the Year Ended December 31,		
Revenue Recognized in the Period from:	**2021**	**2020**	**2019**
Amounts included in deferred revenue at the beginning of the period	$ 23,364	$ 36,032	$ 80,634
Performance obligations satisfied in previous periods	$ 81	$ 25,964	$ 45,592

Mitsubishi Tanabe Pharma Corporation Collaboration Agreement

Summary of Agreement

On December 11, 2015, the Company and MTPC entered into a collaboration agreement, or the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries, collectively, the MTPC Territory. In addition, the Company will supply vadadustat to MTPC for both clinical and commercial use in the MTPC Territory, subject to MTPC's option to manufacture commercial drug product in the MTPC Territory.

The Company and MTPC agreed that, instead of including Japanese patients in the Company's global Phase 3 program for vadadustat, MTPC would be the sponsor of a Phase 3 program for vadadustat in Japan. MTPC was responsible for the costs of the Phase 3 program in Japan and other studies required in Japan, and made no funding payments for the global Phase 3 program for vadadustat. In June 2020, vadadustat was approved in Japan for the treatment of anemia due to CKD, which triggered a $15.0 million regulatory milestone payment to the Company that was received in the third quarter of 2020. In August 2020, MTPC launched vadadustat commercially in Japan under the trade name Vafseo™ as a treatment of anemia due to CKD for adult patients on dialysis and not on dialysis. In January 2022, MTPC filed a new drug application for vadadustat for the treatment of anemia due to CKD in adult patients in Taiwan.

The Company and MTPC have established a joint steering committee pursuant to the MTPC Agreement to oversee development and commercialization of vadadustat in the MTPC Territory, including approval of any development or commercialization plans. Unless earlier terminated, the MTPC Agreement will continue in effect on a country-by-country basis

until the later of the following: expiration of the last-to-expire patent covering vadadustat in such country in the MTPC Territory; expiration of marketing or regulatory exclusivity in such country in the MTPC Territory; or ten years after the first commercial sale of vadadustat in such country in the MTPC Territory. MTPC may terminate the MTPC Agreement upon twelve months' notice at any time after the second anniversary of the effective date of the MTPC Agreement. Either party may terminate the MTPC Agreement upon the material breach of the other party that is not cured within a specified time period or upon the insolvency of the other party.

MTPC is required to make certain milestone payments to the Company aggregating up to approximately $225.0 million upon the achievement of specified development, regulatory and commercial events. More specifically, the Company received $10.0 million in development milestone payments and is eligible to receive up to $40.0 million in regulatory milestone payments, of which the Company received $10.0 million in relation to the Japanese NDA, or JNDA, filing in the third quarter of 2019 and earned an additional $15.0 million following regulatory approval of vadadustat in Japan in the second quarter of 2020, which the Company received in the third quarter of 2020, and up to $175.0 million in commercial milestone payments associated with aggregate sales of all products. In consideration for the exclusive license and other rights contained in the MTPC Agreement, MTPC also made a $20.0 million upfront payment as well as a payment of $20.5 million for Phase 2 studies in Japanese patients completed by the Company and reimbursed by MTPC. The Company is also entitled to receive tiered royalty payments ranging from 13% to 20% on annual net sales of vadadustat in the MTPC Territory. Royalty payments are subject to certain reductions, including upon the introduction of competitive products in certain instances. Royalties are due on a country-by-country basis from the date of first commercial sale of a licensed product in a country until the last to occur of: (i) the expiration of the last to expire valid claim within the intellectual property covering the licensed product, (ii) the expiration of marketing or regulatory exclusivity in such country, or (iii) the tenth anniversary of the first commercial sale of such licensed product in such country. Due to the uncertainty of drug development and commercialization and the high historical failure rates associated therewith, although the Company has received $10.0 million in development milestones and $25.0 million in regulatory milestones, no additional milestone may ever be received from MTPC. The Company recognizes any revenue from MTPC royalties in the period in which the sales occur.

In February 2021, the Company entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or the Royalty Agreement, whereby the Company sold its right to receive royalties and sales milestones under the MTPC Agreement, subject to certain caps and other terms and conditions (see Note 5).

Revenue Recognition

The Company evaluated the elements of the MTPC Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, MTPC, is a customer. The Company's arrangement with MTPC contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop and commercialize vadadustat in the MTPC Territory (the License Deliverable), (ii) clinical supply of vadadustat (the Clinical Supply Deliverable), (iii) knowledge transfer, (iv) Phase 2 dosing study research services (the Research Deliverable), and (v) rights to future know-how.

The Company identified two performance obligations in connection with its material promises under the MTPC Agreement as follows: (i) License, Research and Clinical Supply Performance Obligation and (ii) Rights to Future Know-How Performance Obligation. Factors considered in making the assessment of which material promises will be accounted for as separate performance obligations included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the MTPC Agreement does not include a general right of return.

The Company allocates the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of the standalone selling price for the Rights to Future Know-How Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement and determined it is immaterial. As such, the Company did not develop a best estimate of standalone selling price for the License, Research and Clinical Supply Performance Obligation and allocated the entire transaction price to this performance obligation. The deliverables associated with the License, Research and Clinical Supply Performance Obligation were satisfied as of June 30, 2018.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the estimated cost for the Phase 2 studies, (iii) a non-substantive milestone associated with the first patient enrolled in the NDD-CKD Phase 3 study, and (iv) the cost of all clinical supply provided to MTPC for the Phase 3 studies. No other development and no regulatory milestones were included in the transaction price at inception, as all other milestone amounts were fully constrained. Subsequent to inception, the

transaction price also included certain development and regulatory milestones, as described below. As part of its evaluation of the constraint, the Company considers numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to MTPC and therefore have also been excluded from the transaction price. The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company determined that the remaining consideration that may be payable to the Company subsequent to MTPC's commercial launch of Vafseo™, in the third quarter of 2020 is quarterly royalties on net sales, sales milestones, and certain regulatory milestones.

As of December 31, 2021, the transaction price is comprised of: (i) the up-front payment of $20.0 million, (ii) the cost for the Phase 2 studies of $20.5 million, (iii) the cost of all clinical supply provided to MTPC for the Phase 3 studies, (iv) $10.0 million in development milestones received, (v) $25.0 million in regulatory milestones received, comprised of $10.0 million relating to the JNDA filing and $15.0 million relating to regulatory approval of vadadustat in Japan, and (vi) $1.2 million in royalties from net sales of Vafseo. As of December 31, 2021, all development milestones and $25.0 million in regulatory milestones have been achieved. No other regulatory milestones have been assessed as probable of being achieved and as a result have been fully constrained. Revenue for the License, Research and Clinical Supply Performance Obligation for the MTPC Agreement is being recognized using a proportional performance method, for which all deliverables have been completed. Accordingly, the Company recognized the $15.0 million regulatory milestone relating to regulatory approval of vadadustat in Japan as revenue during the year ended December 31, 2020 and the $10.0 million regulatory milestone for the filing of the JNDA as revenue during the year ended December 31, 2019, as the regulatory milestones were both deemed probable of being achieved and the required performance obligations had been satisfied as of December 31, 2020 and 2019, respectively. The Company recognized $0.8 million and $0.4 million of revenue for royalties from the net sales of Vafseo during the years ended December 31, 2021 and 2020, respectively. As noted above, in February 2021, the Company entered into the Royalty Agreement, whereby the Company sold its right to receive these royalties and sales milestones under the MTPC Agreement, subject to certain caps and other conditions (see Note 5). The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations and comprehensive loss. As of December 31, 2021, there is $0.2 million in accounts receivable, no deferred revenue, and no contract assets. There were no asset or liability balances related to the MTPC Agreement classified as long-term in the consolidated balance sheet as of December 31, 2021.

Supply of Drug Product to MTPC

In March 2020, in connection with the MTPC Agreement, the Company and MTPC executed an amendment to the MTPC Agreement pursuant to which the Company agreed to supply MTPC with certain vadadustat process validation drug product for commercial use, and MTPC agreed to reimburse the Company for certain manufacturing-related expenses. In connection with this arrangement, the Company invoiced the upfront payment of $10.4 million, which it received during the three months ended June 30, 2020. The Company does not recognize revenue under this arrangement until risk of loss passes to MTPC and delivery has occurred and MTPC has accepted the product. During the years ended December 31, 2021 and 2020, the Company recognized $0 million and $6.2 million, respectively, in revenue for drug product that was delivered during the applicable period. As of December 31, 2021, the Company recorded no accounts receivable, no deferred revenue, and $2.1 million in other current liabilities and no other non-current liabilities for drug product that is subject to return by MTPC.

On July 15, 2020, the Company and its collaboration partner MTPC entered into a supply agreement, or the MTPC Supply Agreement. The MTPC Supply Agreement includes the terms and conditions under which the Company will supply vadadustat drug product to MTPC for commercial use in Japan and certain other Asian countries, as contemplated by the MTPC Agreement.

Pursuant to the MTPC Supply Agreement, MTPC provides a rolling forecast, or the MTPC Forecast, to the Company on a quarterly basis. The MTPC Forecast reflects MTPC's needs for vadadustat drug product over a certain number of months, represented as a quantity of vadadustat drug product per calendar quarter. MTPC makes an up-front payment for a certain percentage of each batch of vadadustat drug product ordered. The term of the MTPC Supply Agreement extends throughout the term of the MTPC Agreement, and the termination provisions of the MTPC Agreement govern termination of the MTPC Supply Agreement.

During the year ended December 31, 2021, the Company recognized $11.6 million of revenue under the MTPC Supply Agreement and invoiced MTPC for $18.2 million in up-front payments for vadadustat drug product ordered by MTPC. As of December 31, 2021, the Company recorded $9.4 million in accounts receivable, $7.5 million in deferred revenues, $14.9 million in other current liabilities and $5.8 million in other non-current liabilities.

U.S. Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On December 18, 2016, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement. The collaboration is focused on the development and commercialization of vadadustat in the United States. Under the terms of the Otsuka U.S. Agreement, the Company is responsible for leading the development of vadadustat, including the completed Phase 3 development program, and the Company controls and retains final decision making authority with respect to certain matters, including U.S. pricing strategy and manufacturing. The Company and Otsuka will co-commercialize vadadustat in the United States, subject to the approval of vadadustat by the FDA.

Under the terms of the Otsuka U.S. Agreement, the Company granted to Otsuka a co-exclusive, non-sublicensable license under certain intellectual property controlled by the Company solely to perform medical affairs activities and to conduct non-promotional and commercialization activities related to vadadustat in accordance with the associated plans. The co-exclusive license relates to activities that will be jointly conducted by the Company and Otsuka pursuant to the terms of the Otsuka U.S. Agreement. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the Otsuka U.S. Agreement.

The Company is responsible for performing all activities related to the development of vadadustat as outlined in the current global development plan, while Otsuka may agree to perform certain activities under the global development plan from time to time as agreed to by the parties. The current global development plan encompasses all activities with respect to the completed PRO_2TECT and $INNO_2VATE$ clinical programs through the filing for marketing approval, as well as certain other studies. The Company's obligations related to the conduct of the current global development plan include the associated manufacturing and supply services for vadadustat.

Under the Otsuka U.S. Agreement, the parties jointly conduct all medical affairs, commercialization and non-promotional activities pursuant to underlying plans as agreed to by the parties. If approved by the FDA, Otsuka is obligated to purchase all of its supply requirements of vadadustat for commercial use from the Company pursuant to a separate supply agreement to be negotiated.

The activities under the Otsuka U.S. Agreement are governed by a joint steering committee, or JSC, formed by an equal number of representatives from the Company and Otsuka. The JSC coordinates and monitors the parties' activities under the collaboration. Among other responsibilities, the JSC manages the overall strategic alignment between the parties, oversees the current global development plan and reviews other detailed plans setting forth the parties' activities under the arrangement, including the medical affairs plan and commercialization and non-promotional activities plan. Additionally, the parties established a joint development committee, or JDC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JDC shares information related to, and reviews and discusses activities and progress under, the current global development plan and any other development that may be conducted pursuant to the collaboration. The Company and Otsuka also established a joint manufacturing committee, or JMC, which is comprised of an equal number of representatives from each of the parties. Among other responsibilities, the JMC oversees the manufacturing plan and related manufacturing activities. In support of the potential commercialization of vadadustat, the parties established a joint commercialization committee, or JCC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JCC oversees the activities and progress under the commercialization and non-promotional activities plan and all other sales and marketing activities. The Company has retained final decision-making authority with respect to certain matters, including U.S. pricing strategy and certain other key commercialization matters.

Under the terms of the Otsuka U.S. Agreement, the Company received a $125.0 million up-front, non-refundable, non-creditable cash payment in December 2016. In March 2017, the Company received a payment of approximately $33.8 million, which represented reimbursement for Otsuka's share of costs previously incurred by the Company in implementing the current global development plan through December 31, 2016. Commencing in the third quarter of 2017, whereupon the Company had incurred a specified amount of incremental costs, Otsuka began to contribute, as required by the Otsuka U.S. Agreement, a percentage of the remaining costs incurred under the current global development plan. The Company estimates that Otsuka's funding of the current global development plan costs subsequent to December 31, 2016 will total $360.1 million or more, depending on the actual costs incurred toward the current global development plan, which amount includes the Additional Funding (as defined below). The costs associated with the performance of any development activities in addition to those outlined in the current global development plan will be subject to a cost sharing or reimbursement mechanism as set forth in the Otsuka U.S. Agreement or to be determined by the parties. Costs incurred with respect to medical affairs and commercialization and non-promotional activities will generally be shared equally by the parties. In addition, due to the costs incurred in completing the activities under the current global development plan exceeding a certain threshold in the second quarter of 2019, the Company elected to require Otsuka to increase the aggregate percentage of current global development costs it funds under

the Otsuka U.S. Agreement and the Otsuka International Agreement, as defined below, from 52.5% to 80%, or the Otsuka Funding Option. The Company estimates the additional funding as a result of exercising the Otsuka Funding Option, or the Additional Funding, to total approximately $149.6 million or more, depending on the actual costs incurred toward the current global development plan. The Additional Funding is fully creditable against future payments due to the Company under the arrangement, provided that future payments due to the Company may not be reduced by more than 50% in any calendar year and any remaining creditable amount above 50% in any calendar year will be applied to subsequent future payments until fully credited. As of December 31, 2021, the Additional Funding was $111.9 million.

In addition, Otsuka is required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, as of December 31, 2021, the Company is eligible to receive up to $65.0 million in regulatory milestone payments for the first product to achieve the associated event and up to $575.0 million in commercial milestone payments associated with aggregate sales of licensed products. These future milestones are subject to reduction as a result of the Company's exercise of the Otsuka Funding Option, as described above. Due to the uncertainty of drug development and commercialization and the high historical failure rates associated therewith, no milestone payments may ever be received from Otsuka.

Under the Otsuka U.S. Agreement, the Company and Otsuka also share the costs of commercializing vadadustat in the United States and the profits from the sales of vadadustat after approval by the FDA. In connection with the profit share calculation, net sales include gross sales to third-party customers net of discounts, rebates, chargebacks, taxes, freight and insurance charges and other applicable deductions. Shared costs generally include costs attributable or reasonably allocable to the manufacture of vadadustat for commercialization purposes and the performance of medical affairs activities, non-promotional activities and commercialization activities.

Unless earlier terminated, the Otsuka U.S. Agreement will expire in the United States on a product-by-product basis on the date that one or more generic versions of vadadustat first achieves 90% market penetration. Either party may terminate the Otsuka U.S. Agreement in its entirety upon an uncured breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka U.S. Agreement in its entirety upon 12 months' prior written notice at any time after the release of the first top-line data from the global Phase 3 development program for vadadustat, which release occurred in the second quarter of 2020 with the announcement of top-line data from the INNO$_2$VATE program. In the event of termination of the Otsuka U.S. Agreement, all rights and licenses granted to Otsuka under the Otsuka U.S. Agreement will automatically terminate and the licenses granted to the Company will become freely sublicensable. In addition, the upfront payment, all development costs and milestone payments received by the Company prior to such termination will not be refunded to Otsuka.

Revenue Recognition

The Company evaluated the elements of the Otsuka U.S. Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, Otsuka, is a customer. The Company's arrangement with Otsuka contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop, perform medical affairs activities with respect to and conduct non-promotional and commercialization activities related to vadadustat and products containing or comprising vadadustat (the License Deliverable), (ii) development services to be performed pursuant to the current global development plan (the Development Services Deliverable), (iii) rights to future intellectual property (the Future IP Deliverable), and (iv) joint committee services (the Committee Deliverable).

The Company has identified three performance obligations in connection with its obligations under the Otsuka U.S. Agreement. Factors considered in making the assessment of which material promises will be accounted for as separate performance obligations included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the Otsuka U.S. Agreement does not include a general right of return. The three performance obligations identified in connection with the Company's obligations under the Otsuka U.S. Agreement are as follows:

(i) *License and Development Services Combined (License Performance Obligation)*

The License Deliverable is not distinct from the Development Services Deliverable due to the limitations inherent in the license conveyed. More specifically, the license conveyed to Otsuka does not provide Otsuka with the right to manufacture vadadustat and products containing or comprising vadadustat. However, the manufacturing and supply services that are conducted as part of the services to be performed pursuant to the current global development plan are necessary for Otsuka to fully exploit the associated license for its intended purpose. The value of the rights provided through the license conveyed will be realized when the underlying products covered by the intellectual property progress through the development cycle, receive

regulatory approval and are commercialized. Products containing or comprising vadadustat cannot be commercialized until the development services under the current global development plan are completed. Accordingly, Otsuka must obtain the manufacturing and supply of the associated products that are included within the development services to be performed pursuant to the current global development plan from the Company in order to derive benefit from the license, which significantly limits the ability for Otsuka to utilize the License Deliverable for its intended purpose in a way that generates economic benefits.

(i) *Rights to Future Intellectual Property (Future IP Performance Obligation)*

The License Deliverable and the Development and Services Deliverable combined are distinct from the Future IP Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the receipt of any other intellectual property that may be discovered or developed in the future. The Future IP Deliverable is distinct from the Committee Deliverable because the joint committee services have no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Future IP Deliverable qualifies as a separate performance obligation.

(i) *Joint Committee Services (Committee Performance Obligation)*

The License Deliverable and the Development and Services Deliverable combined are distinct from the Committee Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the joint committee services. The Committee Deliverable also is distinct from the rights to Future IP Deliverable because the joint committee services have no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Committee Deliverable qualifies as a separate performance obligation.

The Company allocates the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of standalone selling price for the Committee Performance Obligation after considering the nature of the services to be performed and estimates of the associated effort and rates applicable to such services that would be expected to be realized under similar contracts. The Company developed a best estimate of standalone selling price for the Future IP Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement. The Company did not develop a best estimate of standalone selling price for the License Performance Obligation due to the following: (i) the best estimates of standalone selling price associated with the Future IP Performance Obligation was determined to be immaterial and (ii) the period of performance and pattern of recognition for the License Performance Obligation and the Committee Performance Obligation was determined to be similar. The Company has concluded that a change in the key assumptions used to determine the best estimate of standalone selling price for each performance obligation would not have a significant impact on the allocation of arrangement consideration.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the cost share payment with respect to amounts incurred by the Company through December 31, 2016, and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to December 31, 2016. No development or regulatory milestones were included in the transaction price at inception, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Otsuka and therefore have also been excluded from the transaction price.

The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company determined that under ASC 606, the contract was modified in the second quarter of 2019 when the Otsuka Funding Option became effective and the Company became eligible to receive the Additional Funding amount. In connection with the modification, the Company adjusted the transaction price to include the Additional Funding amount as additional variable consideration. The Company constrains the variable consideration to an amount for which a significant revenue reversal is not probable. In the event that there is consideration received by a customer in the form of activities performed by such customer under the global development plan, such consideration is reflected as a reduction to the transaction price as contra revenue rather than as an expense because the associated services are not distinct from the License Performance Obligation.

No amounts were allocated to the Future IP Performance Obligation because the associated best estimate of standalone selling price was determined to be immaterial. Due to the similar performance period and recognition pattern between the License Performance Obligation and the Committee Performance Obligation, the transaction price has been allocated to the License Performance Obligation and the Committee Performance Obligation on a combined basis. Accordingly, the Company will

recognize revenue related to the allocable arrangement consideration on a proportional performance basis as the underlying development services are performed pursuant to the current global development plan which is commensurate with the period and consistent with the pattern over which the Company's obligations are satisfied for both the License Performance Obligation and the Committee Performance Obligation. Effectively, the Company has treated the arrangement as if the License Performance Obligation and the Committee Performance Obligation are a single performance obligation.

As of December 31, 2021, the transaction price totaling $518.9 million is comprised of: (i) the up-front payment of $125.0 million, (ii) the cost share payment with respect to amounts incurred by the Company through December 31, 2016 of $33.8 million, and (iii) the estimate of the net cost share consideration to be received of approximately $360.1 million with respect to amounts incurred by the Company subsequent to December 31, 2016. As of December 31, 2021, no development or regulatory milestones have been assessed as probable of being reached and thus have been fully constrained.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized revenue totaling approximately $36.6 million, $93.4 million and $131.3 million, respectively, with respect to the Otsuka U.S. Agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations. As of December 31, 2021, there is approximately $20.4 million of deferred revenue related to the Otsuka U.S. Agreement of which $8.0 million is classified as current and $12.4 million is classified as long-term in the accompanying consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of December 31, 2021, there are approximately $2.0 million in contract liabilities (included in accounts payable) and $3.0 million in prepaid expenses and other current assets in the accompanying consolidated balance sheet. As of December 31, 2021, there were no accounts receivable in the accompanying consolidated balance sheet.

The Company determined that the medical affairs, commercialization and non-promotional activities elements of the Otsuka U.S. Agreement represent joint operating activities in which both parties are active participants and of which both parties are exposed to significant risks and rewards that are dependent on the success of the activities. Accordingly, the Company is accounting for the joint medical affairs, commercialization and non-promotional activities in accordance with ASC No. 808, *Collaborative Arrangements* (ASC 808). Additionally, the Company has determined that in the context of the medical affairs, commercialization and non-promotional activities, Otsuka does not represent a customer as contemplated by ASC 606-10-15, *Revenue from Contracts with Customers – Scope and Scope Exceptions*. As a result, the activities conducted pursuant to the medical affairs, commercialization and non-promotional activities plans will be accounted for as a component of the related expense in the period incurred. During the years ended December 31, 2021, 2020 and 2019, the Company incurred approximately $17.5 million, $5.1 million and $1.8 million, respectively, of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement of which approximately $8.6 million, $2.2 million and $0.7 million are reimbursable by Otsuka and recorded as a reduction to research and development expense during each of the years ended December 31, 2021, 2020 and 2019, respectively. During the years ended December 31, 2021, 2020 and 2019, Otsuka incurred approximately $0.9 million, $2.1 million and $1.9 million, respectively, of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, of which approximately $0.4 million, $1.1 million and $1.0 million are reimbursable by the Company and recorded as an increase to research and development expense during the years ended December 31, 2021, 2020 and 2019, respectively.

International Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On April 25, 2017, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka International Agreement. The collaboration is focused on the development and commercialization of vadadustat in Europe, Russia, China, Canada, Australia, the Middle East and certain other territories, collectively, the Otsuka International Territory. Under the terms of the Otsuka International Agreement, the Company is responsible for leading the development of vadadustat, including the completed global Phase 3 development program. Otsuka has the sole responsibility, at its own cost, for the commercialization of vadadustat in the Otsuka International Territory, subject to the approval by the relevant regulatory authorities.

Under the terms of the Otsuka International Agreement, the Company granted to Otsuka an exclusive, sublicensable license under certain intellectual property controlled by the Company to develop and commercialize vadadustat and products containing or comprising vadadustat in the Otsuka International Territory.

Pursuant to the terms of the Otsuka International Agreement, the Company is responsible for performing all activities related to the development of vadadustat as outlined in the current global development plan, while Otsuka may agree to perform certain activities under the global development plan from time to time as agreed to by the parties. Under the Otsuka International Agreement, the Company controls and retains final decision-making authority with respect to certain matters. Per the terms of the Otsuka International Agreement, Otsuka is generally responsible for the conduct of any development activities that may be

required for marketing approvals in the Otsuka International Territory or otherwise performed with respect to the Otsuka International Territory that are incremental to those included in the current global development plan. The Company's obligations related to the conduct of the current global development plan include the associated manufacturing and supply services for vadadustat.

Under the Otsuka International Agreement, Otsuka is to be solely responsible for the conduct of all medical affairs and commercialization activities in the Otsuka International Territory pursuant to underlying plans as reviewed and discussed by the parties. If approved by the relevant jurisdictional regulatory health authorities in the Otsuka International Territory, the Company will provide vadadustat to Otsuka for commercialization pursuant to a separate supply agreement to be negotiated. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

The activities under the Otsuka International Agreement are governed by a JSC formed by an equal number of representatives from the Company and Otsuka. The JSC coordinates and monitors the parties' activities under the collaboration. Among other responsibilities, the JSC manages the overall strategic alignment between the parties, oversees the current global development plan and reviews other detailed plans setting forth any other development activities that may be conducted under the arrangement. Additionally, the parties established a JDC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JDC shares information related to, and reviews and discusses activities and progress under, the current global development plan and any other development that may be conducted pursuant to the collaboration. The Company and Otsuka also established a JMC, which is comprised of an equal number of representatives from each of the parties. Among other responsibilities, the JMC oversees the manufacturing plan and related manufacturing activities. In support of the potential commercialization of vadadustat, the parties established a JCC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JCC manages the activities and progress under the commercialization and non-promotional activities plan and all other sales and marketing activities. The Company has retained final decision-making authority with respect to certain matters. Otsuka has retained final decision-making authority with respect to all commercialization matters, other than decisions related to certain marketing matters.

Under the terms of the Otsuka International Agreement, the Company received a $73.0 million up-front, non-refundable, non-creditable cash payment. The Company also received a payment of approximately $0.2 million which represents reimbursement for Otsuka's share of costs previously incurred by the Company in implementing the current global development plan in excess of a specified threshold during the quarter ended March 31, 2017. Commencing in the second quarter of 2017, Otsuka began to contribute, as required by the Otsuka International Agreement, a percentage of the remaining costs incurred under the current global development plan. The Company estimates that Otsuka's funding of the current global development plan costs subsequent to March 31, 2017 will total roughly $244.6 million or more, depending on the actual current global development plan costs incurred. The costs associated with the performance of any mutually agreed upon development activities in addition to those outlined in the current global development plan will be subject to a cost sharing or reimbursement mechanism as set forth in the Otsuka International Agreement or to be determined by the parties. Otsuka may elect to conduct additional studies of vadadustat in the EU, subject to the Company's right to delay such studies based on its objectives outside the Otsuka International Territory. Otsuka will pay a percentage of the costs of any such studies, and the Company will pay its portion of the costs in the form of a credit against future amounts due to the Company under the Otsuka International Agreement. The costs incurred related to any other development activities, which are pursued solely for obtaining or maintaining marketing approval in the Otsuka International Territory or otherwise performed solely with respect to the Otsuka International Territory that are incremental to the development activities included in the current global development plan, will be borne in their entirety by Otsuka. Otsuka will pay costs incurred with respect to medical affairs and commercialization activities in the Otsuka International Territory.

In addition, Otsuka would be required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, as of December 31, 2021, the Company is eligible to receive up to $17.0 million in regulatory milestone payments for the licensed HIF product if the Company achieves the associated event within 12 to 24 months of the first HIF product approval. Moreover, the Company is eligible for up to $525.0 million in commercial milestone payments associated with aggregate sales of all licensed products. Additionally, to the extent vadadustat is commercialized, the Company would be entitled to receive tiered royalty payments ranging from the low double digits to the low thirties based on a percentage of net sales. Royalties are due on a country-by-country basis from the date of the first commercial sale of a licensed product in a country until the latest to occur of: (i) the expiration date in such country of the last to expire valid claim within the intellectual property covering the licensed product, (ii) the date of expiration of data or regulatory exclusivity in such country or (iii) the tenth anniversary of the first commercial sale of such licensed product in such country. Due to the uncertainty of pharmaceutical development and the high historical failure rates associated therewith, no milestone or royalty payments may ever be received from Otsuka. There are no cancellation, termination or refund provisions in the Otsuka International Agreement that contain material financial consequences to the Company.

Unless earlier terminated, the Otsuka International Agreement will expire upon the expiration of the royalty term in the last country in the Otsuka International Territory. Either party may terminate the Otsuka International Agreement in its entirety upon an uncured material breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka International Agreement in its entirety or for a specific region in the Otsuka International Territory upon 12 months' prior written notice at any time after the release of the first top-line data from the global Phase 3 development program for vadadustat, which release occurred in the second quarter of 2020 with the announcement of top-line data from the $INNO_2VATE$ program. In the event of termination of the Otsuka International Agreement, all rights and licensees granted to Otsuka under the Otsuka International Agreement will automatically terminate, and the licenses granted to the Company will become freely sublicensable, but potentially subject to a future royalty. In addition, the upfront payment, all development costs and milestone payments received by the Company prior to such termination will not be eligible for refund to Otsuka.

Revenue Recognition

The Company has accounted for the Otsuka International Agreement separately from the collaboration arrangement with Otsuka with respect to the U.S. due to the lack of interrelationship and interdependence of the elements and payment terms within each of the contracts as they relate to the respective territories. Accordingly, the Company has applied the guidance in ASC 606 solely in reference to the terms and conditions of the Otsuka International Agreement, while the Otsuka U.S. Agreement has continued to be accounted for as a discrete agreement in its own right. The Company evaluated the Otsuka International Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, Otsuka, is a customer. The Company's arrangement with Otsuka related to the Otsuka International Territory contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop and commercialize (including the associated packaging) vadadustat and products containing or comprising vadadustat and development services to be performed pursuant to the current global development plan (the License and Development Services Deliverable), (ii) rights to future intellectual property (the Future IP Deliverable) and (iii) joint committee services (the Committee Deliverable).

The Company has identified three performance obligations in connection with its obligations under the Otsuka International Agreement. Factors considered in making this assessment of which material promises will be accounted for as a separate performance obligation included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the Otsuka International Agreement does not include a general right of return. The three performance obligations identified in connection with the Company's obligations under the Otsuka International Agreement are as follows:

(i) *License and Development Services Combined (License Performance Obligation)*

The Company has determined that the license granted to Otsuka pursuant to the Otsuka International Agreement will be accounted for as component of the development services as opposed to a separately identified promise. Although the rights granted under the license are effective throughout the entire term of the arrangement, the Company will not be providing significant additional contributions of study data, regulatory submissions and regulatory approvals beyond the point that services under the current global development plan are conducted. Therefore, the period and pattern of recognition would be the same for both the license and the development services. Consequently, the Company has concluded that the license will effectively be treated as an inherent part of the associated development services promise instead of as a separate promise. As a result, the License and Development Services Deliverable will be treated as a single performance obligation (the License Performance Obligation).

(i) *Rights to Future Intellectual Property (Future IP Performance Obligation)*

The License and Development Services Deliverable is distinct from the Future IP Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the receipt of any other intellectual property that may be discovered or developed in the future. The Future IP Deliverable is distinct from the Committee Deliverable because the Committee Deliverable has no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Future IP Deliverable qualifies as a separate performance obligation.

(i) *Joint Committee Services (Committee Performance Obligation)*

The License and Development Services Deliverable is distinct from the Committee Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development service without the joint committee services. The Committee Deliverable is distinct from the Future IP Deliverable because the Committee Deliverable has no bearing on the value to be derived from the rights to potential

future intellectual property. As a result, the Committee Deliverable qualifies as a separate performance obligation.

The Company allocates the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of standalone selling price for the Committee Performance Obligation after considering the nature of the services to be performed and estimates of the associated effort and rates applicable to such services that would be expected to be realized under similar contracts. The Company developed a best estimate of standalone selling price for the Future IP Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement. The Company did not develop a best estimate of standalone selling price for the License Performance Obligation due to the following: (i) the best estimates of standalone selling price associated with the Future IP Performance Obligation was determined to be immaterial and (ii) the period of performance and pattern of recognition for the License Performance Obligation and the Committee Performance Obligation was determined to be similar. The Company has concluded that a change in the key assumptions used to determine the best estimate of standalone selling price for each performance obligation would not have a significant impact on the allocation of arrangement consideration.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the cost share payment with respect to amounts incurred by the Company during the quarter ended March 31, 2017, and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to March 31, 2017. No development or regulatory milestones were included in the transaction price at inception, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including whether the receipt of the milestone payment is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Otsuka and therefore have also been excluded from the transaction price.

The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. In the event that there is consideration received by a customer in the form of activities performed by such customer under the global development plan, such consideration is reflected as a reduction to the transaction price as contra revenue rather than as an expense because the associated services are not distinct from the License Performance Obligation.

No amounts were allocated to the Future IP Performance Obligation because the associated best estimate of standalone selling price was determined to be immaterial. Due to the similar performance period and recognition pattern between the License Performance Obligation and the Committee Performance Obligation, the transaction price has been allocated to the License Performance Obligation and the Committee Performance Obligation on a combined basis. Accordingly, the Company will recognize revenue related to the allocable arrangement consideration on a proportional performance basis as the underlying development services are performed pursuant to the current global development plan which is commensurate with the period and consistent with the pattern over which the Company's obligations are satisfied for both the License Performance Obligation and the Committee Performance Obligation. Effectively, the Company has treated the arrangement as if the License Performance Obligation and the Committee Performance Obligation are a single performance obligation.

As of December 31, 2021, the transaction price totaling $317.7 million is comprised of: (i) the up-front payment of $73.0 million, (ii) the cost share payment with respect to amounts incurred by the Company during the quarter ended March 31, 2017 of $0.2 million, and (iii) an estimate of the net cost share consideration to be received with respect to amounts incurred by the Company subsequent to March 31, 2017 of $244.6 million. As of December 31, 2021, no development or regulatory milestones have been assessed as probable of being reached and thus have been fully constrained.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized revenue totaling approximately $16.4 million, $45.5 million, and $75.6 million, respectively, with respect to the Otsuka International Agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations. As of December 31, 2021, there is approximately $9.9 million of deferred revenue related to the Otsuka International Agreement of which $5.5 million is classified as current and $4.4 million is classified as long-term in the accompanying consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of December 31, 2021, there are $0.9 million in contract liabilities (included in accounts payable) and $1.3 million in prepaid expenses and other current assets in the accompanying consolidated balance sheet. As of December 31, 2020, there were no accounts receivable in the accompanying consolidated balance sheet.

Janssen Pharmaceutica NV Research and License Agreement

Summary of Agreement

On February 9, 2017, the Company entered into a Research and License Agreement, the Janssen Agreement, with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, pursuant to which Janssen granted the Company an exclusive license under certain intellectual property rights to develop and commercialize worldwide certain HIF prolyl hydroxylase targeted compounds.

Under the terms of the Janssen Agreement, Janssen granted to the Company a license for a three-year research term to conduct research on the HIF compound portfolio, which research term is now expired. During the research term, the Company could designate one or more compounds as candidates for development and commercialization. Once a compound was designated for development and commercialization, the Company was to be solely responsible for the development and commercialization of the compound worldwide at its own cost and expense.

Under the terms of the Janssen Agreement, the Company made an upfront payment of $1.0 million in cash to Janssen and issued a warrant to purchase 509,611 shares of the Company's common stock, which expired on February 9, 2022. In addition, Janssen could be eligible to receive up to an aggregate of $16.5 million from the Company in specified development milestone payments on a product-by-product basis. Janssen will also be eligible to receive up to $215.0 million from the Company in specified commercial milestones as well as tiered, escalating royalties ranging from a low to mid-single digit percentage of net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory.

Unless earlier terminated, the Janssen Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longer of the expiration of the patents licensed under the Janssen Agreement, the expiration of regulatory exclusivity for such product, or 10 years from first commercial sale of such product. The Company may terminate the Janssen Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Janssen. The parties also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Janssen Agreement or in the event of certain additional circumstances.

As discussed above, the Company issued a Common Stock Purchase Warrant, or the Warrant, to Johnson & Johnson Innovation – JJDC, Inc., or JJDC, an affiliate of Janssen, for 509,611 shares of the Company's common stock at an exercise price of $9.81 per share. The Warrant was exercisable by JJDC, in whole or in part, at any time prior to February 9, 2022. The Company recorded the fair value of the Warrant in the amount of $3.4 million to additional paid-in capital and research and development expense in March 2017. The Warrant expired on February 9, 2022.

Cyclerion Therapeutics License Agreement

Summary of Agreement

On June 4, 2021, the Company entered into a License Agreement, the Cyclerion Agreement, with Cyclerion Therapeutics Inc., or Cyclerion, pursuant to which Cyclerion granted the Company an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase ("sGC") stimulator.

Under the terms of the Cyclerion Agreement, the Company made an upfront payment of $3.0 million in cash to Cyclerion, which was paid during the second quarter of 2021. Substantially all of the fair value of the assets acquired in conjunction with the Cyclerion Agreement was concentrated in the acquired license. As a result, the Company accounted for this transaction as an asset acquisition under ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business*. The upfront payment was charged to expense at acquisition, as it relates to a development stage compound with no alternative future use.

In addition, Cyclerion is eligible to receive up to an aggregate of $222.0 million from the Company in specified development and regulatory milestone payments on a product-by-product basis. Cyclerion will also be eligible to receive specified commercial milestones as well as tiered royalties ranging from a low-single-digit to mid-double-digit percentage of net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory. The Company recorded the upfront payment in the amount of $3.0 million to research and development expense in June 2021.

Unless earlier terminated, the Cyclerion Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longest of (i) the expiration of the patents licensed under the Cyclerion Agreement, (ii) the expiration of regulatory exclusivity for such product, and (iii) 10 years from first commercial sale of such product. The Company may terminate the Cyclerion Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Cyclerion. The parties also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Cyclerion Agreement or in the event of certain additional circumstances.

Vifor License Agreement

Summary of Agreement

On May 12, 2017, the Company entered into a License Agreement, or the Vifor Agreement, with Vifor (International) Ltd., or Vifor Pharma, pursuant to which the Company granted Vifor Pharma an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, an affiliate of Fresenius Medical Care North America, or FMCNA, in the United States. On April 8, 2019, the Company and Vifor Pharma entered into an Amended and Restated License Agreement, or the Vifor First Amended Agreement, which amended and restated in full the Vifor Agreement.

Pursuant to the Vifor First Amended Agreement, the Company granted Vifor Pharma an exclusive license to sell vadadustat to FKC and to certain third party dialysis organizations approved by the Company, or Third Party Dialysis Organizations, in the United States.

The license granted under the Vifor First Amended Agreement was to become effective upon (i) the approval of vadadustat for DD-CKD adult patients by the FDA, (ii) the earlier of a determination by the Centers for Medicare & Medicaid Services, or CMS, that vadadustat will be reimbursed using Medicare's bundled reimbursement model or that vadadustat will be reimbursed using the Transitional Drug Add-On Payment Adjustment, and (iii) payment by Vifor Pharma of a $25.0 million milestone upon the occurrence of (i) and (ii).

The Vifor First Amended Agreement is structured as a profit share arrangement between the Company and Vifor Pharma in which the Company will receive a majority of the profit, after deduction of certain amounts relating to Vifor Pharma's costs, from Vifor Pharma's sales of vadadustat to FKC and the Third Party Dialysis Organizations in the United States. The Company will share the milestone payment and the revenue from the profit share with Otsuka pursuant to the Otsuka U.S. Agreement. Under the Vifor First Amended Agreement, the Company retains rights to commercialize vadadustat for use in the NDD-CKD market and in other dialysis organizations in the United States, which will be done in collaboration with Otsuka following FDA approval.

The Vifor First Amended Agreement provides that the Company and Vifor Pharma will enter into a commercial supply agreement for vadadustat pursuant to which the Company will supply all of Vifor Pharma's requirements for vadadustat in the United States. In addition, Vifor Pharma will enter into supply arrangements with FKC and the Third Party Dialysis Organizations that will govern the terms pursuant to which Vifor Pharma will supply vadadustat to FKC and the Third Party Dialysis Organizations for use in patients at its dialysis centers in the United States. During the term of the Vifor First Amended Agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the United States to FKC or its affiliates or to any Third Party Dialysis Organization, and the Company may not directly supply vadadustat to FKC or any other affiliate of FMCNA or any Third Party Dialysis Organization.

Unless earlier terminated, the Vifor First Amended Agreement will expire upon the later of the expiration of all patents that claim or cover vadadustat or expiration of marketing or regulatory exclusivity for vadadustat in the United States. Vifor Pharma may terminate the Vifor First Amended Agreement in its entirety upon 12 months' prior written notice after the release of the first top-line data in the vadadustat global Phase 3 program for DD-CKD adult patients, which release occurred in the second quarter of 2020 with the announcement of top-line data from the INNO$_2$VATE program. In addition, either party may, subject to a cure period, terminate the Vifor First Amended Agreement in the event of the other party's uncured material breach or bankruptcy. The Company may terminate the Vifor First Amended Agreement (or suspend the license) upon the occurrence of certain events, such as for specific violations of the Vifor First Amended Agreement, Vifor Pharma's failure to achieve certain sales levels, or if there are changes in Vifor Pharma's relationship with FKC or in applicable laws and regulations related to the reimbursement of drugs like vadadustat at dialysis clinics, or if Vifor Pharma contests the validity or enforceability of any patent controlled by the Company that covers vadadustat. The Vifor First Amended Agreement also includes a standstill provision and customary representations and warranties.

The Vifor First Amended Agreement was further amended on February 18, 2022, which amended and restated the Vifor First Amended Agreement in its entirety. See Note 18 contained in this Annual Report on Form 10-K for further information.

Investment Agreement

In connection with the Vifor Agreement, in May 2017, the Company and Vifor Pharma entered into an investment agreement, or the First Investment Agreement, pursuant to which the Company sold an aggregate of 3,571,429 shares of the Company's common stock, or the Shares, to Vifor Pharma at a price per share of $14.00 for a total of $50.0 million. The amount representing the premium over the closing stock price of $12.69 on the date of the transaction, totaling $4.7 million, was determined by the Company to represent consideration related to the Vifor Agreement.

As the parties' rights under the Vifor Agreement are conditioned upon (a) the approval of vadadustat for DD-CKD adult patients by the FDA; (b) the earlier of a determination by CMS that vadadustat will be reimbursed using Medicare's bundled reimbursement model or that vadadustat will be reimbursed using the Transitional Drug Add-On Payment Adjustment; and (c) payment by Vifor Pharma of a $25.0 million milestone upon the occurrence of (a) and (b), in accordance with ASC 606, the Company has determined that the full transaction price is fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including clinical and regulatory risks that must be overcome in order for the parties' rights to become effective and the probability of the $25.0 million milestone being achieved. Accordingly, the $4.7 million continues to be recorded as deferred revenue in the accompanying consolidated balance sheets. Upon the satisfaction of the aforementioned conditions, revenue will be recognized as the Company supplies vadadustat to Vifor Pharma using a proportional performance method.

Vifor Pharma agreed to a lock-up restriction such that it agreed not to sell the Shares for a period of time following the effective date of the First Investment Agreement as well as a customary standstill agreement. The lock-up restriction in place as part of the First Investment Agreement has since expired. In addition, the First Investment Agreement contains voting agreements made by Vifor Pharma with respect to the Shares. The Shares have not been registered pursuant to the Securities Act, and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Securities Act and Rule 506 promulgated thereunder.

The Company and Vifor Pharma also entered into a new Investment Agreement on February 18, 2022. See Note 18 contained in this Annual Report on Form 10-K for further information.

Priority Review Voucher Letter Agreement

On February 14, 2020, the Company entered into a letter agreement, or the Letter Agreement, with Vifor Pharma relating to Vifor Pharma's agreement with a third party to purchase a Priority Review Voucher, or the PRV, issued by the FDA, subject to satisfaction of customary closing conditions, or the PRV Purchase. A PRV entitles the holder to priority review of a New Drug Application, or NDA, or a Biologics License Application for a new drug, which reduces the target FDA review time to six months after official acceptance of the submission, and could lead to expedited approval. Pursuant to the Letter Agreement, Akebia paid Vifor Pharma $10.0 million in connection with the closing of the PRV Purchase. The $10.0 million payment to Vifor Pharma was recorded to research and development expense in the consolidated statement of operations and as an operating cash outflow in the unaudited condensed consolidated statement of cash flows during 2020. Vifor Pharma was obligated to retain all rights to, and maintain the validity of, the PRV until Akebia and Vifor Pharma (a) enter into a definitive agreement setting forth the financial and other terms by which Vifor Pharma will assign the PRV to Akebia for use with Akebia's planned NDA for vadadustat for the treatment of anemia due to CKD in both dialysis-dependent and non-dialysis dependent patients, or (b) make a mutual decision to sell the PRV and share the proceeds based on certain terms. In March 2021, the Company submitted an NDA for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. The Company's NDA submission did not include a PRV.

On August 21, 2021, the Company and Vifor Pharma executed an amendment to the Letter Agreement whereby the parties agreed that Vifor Pharma would sell the PRV to a third party, and the Company and Vifor Pharma would share the proceeds from the sale based on certain terms. In the fourth quarter of 2021, Vifor Pharma sold the PRV to a third party, and Vifor Pharma paid the Company $8.6 million in proceeds from the sale, which was recorded as contra research and development expense. These proceeds were subsequently paid to Otsuka as reimbursement for their contribution to the purchase of the PRV, as required under a separate letter agreement executed with Otsuka.

License Agreement with Panion & BF Biotech, Inc.

As a result of the Merger, the Company had a license agreement, which was amended from time to time, with Panion & BF Biotech, Inc., or Panion, under which Keryx, the Company's wholly owned subsidiary, was the contracting party, or the Panion License Agreement, pursuant to which Keryx in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, or the Licensor Territory, for the development and commercialization of ferric citrate.

On April 17, 2019, the Company and Panion entered into a second amended and restated license agreement, or the Panion Amended License Agreement, which amends and restates in full the Panion License Agreement, effective as of April 17, 2019. The Panion Amended License Agreement provides Keryx with an exclusive license under Panion-owned know-how and patents covering the rights to sublicense, develop, make, use, sell, offer for sale, import and export ferric citrate worldwide, excluding the Licensor Territory. The Panion Amended License Agreement also provides Panion with an exclusive license under Keryx-owned patents covering the rights to sublicense (with the Company's written consent), develop, make, use, sell, offer for sale, import and export ferric citrate in certain countries in the Licensor Territory. Consistent with the Panion License Agreement, under the Panion Amended License Agreement, Panion is eligible to receive from the Company or any sublicensee royalty payments based on a mid-single digit percentage of sales of ferric citrate in the Company's licensed territories. The Company is eligible to receive from Panion or any sublicensee royalty payments based on a mid-single digit percentage of net sales of ferric citrate in Panion's licensed territories.

The Panion Amended License Agreement terminates upon the expiration of each of the Company's and Panion's obligations to pay royalties thereunder. In addition, the Company may terminate the Panion Amended License Agreement (i) in its entirety or (ii) with respect to one or more countries in the Company's licensed territory, in either case upon 90 days' notice. The Company and Panion also each have the right to terminate the Panion Amended License Agreement upon the occurrence of a material breach of the Panion Amended License Agreement by the other party, subject to certain cure provisions, or certain insolvency events. The Panion Amended License Agreement also provides that, on a country-by-country basis, until the second anniversary of the expiration of the obligation of the Company or Panion, as applicable, to pay royalties in a country in which such party has ferric citrate for sale on the date of such expiration, neither the other party nor its affiliates will, directly or indirectly, sell, distribute or otherwise commercialize or supply or cause to supply ferric citrate to a third party for sale or distribution in such country.

The Panion Amended License Agreement includes customary terms relating to, among others, indemnification, confidentiality, remedies, and representations and warranties. In addition, the Panion Amended License Agreement provides that each of the Company and Panion has the right, but not the obligation, to conduct litigation against any infringer of certain patent rights under the Panion Amended License Agreement in certain territories.

During the years ended December 31, 2021, 2020 and 2019, the Company incurred approximately $11.8 million, $11.2 million and $10.2 million, respectively, in royalty payments due to Panion relating to the Company's sales of Auryxia in the United States and JT and Torii's net sales of Riona in Japan.

Sublicense Agreement with Japan Tobacco, Inc. and its subsidiary, Torii Pharmaceutical Co., Ltd.

Summary of Agreement

As a result of the Merger, the Company has an Amended and Restated Sublicense Agreement, which was amended in June 2013, with JT and Torii, or the JT and Torii Sublicense Agreement, under which Keryx, the Company's wholly owned subsidiary, remains the contracting party. Under the JT and Torii Sublicense Agreement, JT and Torii obtained the exclusive sublicense rights for the development and commercialization of ferric citrate hydrate in Japan. JT and Torii are responsible for the future development and commercialization costs in Japan.

In January 2014, JT and Torii received manufacturing and marketing approval of ferric citrate from the Japanese Ministry of Health, Labour and Welfare. Ferric citrate hydrate, which launched in May 2014 and is being marketed in Japan by Torii under the brand name Riona, is indicated as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including NDD-CKD and DD-CKD. In July 2019, JT and Torii, reported positive top-line results from a pivotal Phase 3 comparative study evaluating Riona for the treatment of IDA in adult patients in Japan, which was approved in March 2021. In May 2020, JT and Torii filed an application for approval of IDA as an additional indication for Riona in Japan. The Company is eligible to receive royalty payments based on a tiered low double-digit percentage of net sales of Riona in Japan inclusive of amounts that the Company must pay to Panion on JT and Torii's net sales of Riona under the Panion License Agreement subject to certain reductions upon expiration or termination of the Amended and Restated License Agreement between Keryx and Panion, pursuant to which Keryx in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, for the development and commercialization of ferric citrate. The Company is entitled to receive up to an additional $55.0 million upon the achievement of certain annual net sales milestones.

The sublicense under the JT and Torii Sublicense Agreement terminates upon the expiration of all underlying patent rights. Also, JT and Torii may terminate the JT and Torii Sublicense Agreement with or without cause upon at least six months prior written notice to the Company. Additionally, either party may terminate the JT and Torii Sublicense Agreement for cause upon 60 days' prior written notice after the breach of any uncured material provision of the JT and Torii Sublicense Agreement, or after certain insolvency events.

Revenue Recognition

The Company evaluated the elements of the JT and Torii Sublicense Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, JT and Torii, is a customer. The Company's arrangement with JT and Torii contains the following material promises under the contract at inception: (i) exclusive license to develop and commercialize ferric citrate hydrate in Japan (the License Deliverable), (ii) supply of ferric citrate hydrate until JT and Torii could secure their own source (the Supply Deliverable), (iii) knowledge transfer, and (iv) rights to future know-how.

The Company identified two performance obligations in connection with its obligations under the JT and Torii Sublicense Agreement: (i) *License and Supply Performance Obligation* and (ii) *Rights to Future Know-How Performance Obligation*. The Company allocated the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of the standalone selling price for the Rights to Future Know-How Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement and determined it immaterial. As such, the Company did not develop a best estimate of standalone selling price for the License and Supply Performance Obligation and allocated the entire transaction price to this performance obligation. Additionally, as of the consummation of the Merger, the services associated with the License and Supply Performance Obligation were completed and JT and Torii had secured their own source to manufacture ferric citrate hydrate. As such, any initial license fees as well as any development-based milestones and manufacturing fee revenue were received and recognized prior to the Merger. The Company determined that the remaining consideration that may be payable to the Company under the terms of the sublicense agreement are either quarterly royalties on net sales or payments due upon the achievement of sales-based milestones. In accordance with ASC 606, the Company recognizes sales-based royalties and milestone payments based on the level of sales, when the related sales occur as these amounts have been determined to relate predominantly to the license granted to JT and Torii and therefore are recognized at the later of when the performance obligation is satisfied, or the related sales occur.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized $5.8 million, $5.7 million and $5.9 million, respectively, in license revenue related to royalties earned on net sales of Riona in Japan. The Company records the associated mid-single digit percentage of net sales royalty expense due to Panion, the licensor of Riona, in the same period as the royalty revenue from JT and Torii is recorded.

5. Liability Related to Sale of Future Royalties

On February 25, 2021, the Company entered into the Royalty Agreement with HealthCare Royalty Partners IV, L.P., or HCR, pursuant to which the Company sold to HCR its right to receive royalties and sales milestones for vadadustat in Japan and certain other Asian countries, such countries, collectively, the MTPC Territory, and such payments collectively the Royalty Interest Payments, in each case, payable to the Company under the MTPC Agreement, subject to an annual maximum "cap" of $13.0 million, or the Annual Cap, and an aggregate maximum "cap" of $150.0 million, or the Aggregate Cap. After HCR receives Royalty Interest Payments equal to the Annual Cap in a given calendar year, the Company will receive 85% of the Royalty Interest Payments for the remainder of that year. After HCR receives Royalty Interest Payments equal to the Aggregate Cap, or the Company pays the Aggregate Cap to HCR (net of the Royalty Interest Payments already received by HCR), the Royalty Interest Payments will revert back to the Company, and HCR would have no further right to any Royalty Interest Payments. The Company received $44.8 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and the Company is eligible to receive an additional $5.0 million in each year from 2021 through 2023 under the Royalty Agreement if specified annual sales milestones are achieved for vadadustat in the MTPC Territory, subject to the satisfaction of certain customary conditions. The sales milestone for vadadustat in the MTPC Territory was not achieved for 2021. The Company retains the right to receive all potential future regulatory milestones for vadadustat under the MTPC Agreement. The Royalty Agreement will terminate on the earlier of the date on which HCR has received (i) the last Royalty Interest Payment or (ii) payment by the Company of an amount equal to the Aggregate Cap minus the aggregate amount of all Royalty Interest Payments actually received by HCR.

Although the Company sold its right to receive royalties and sales milestones for vadadustat in the MTPC Territory as described above, as a result of its ongoing involvement in the cash flows related to these royalties, the Company will continue to account for these royalties as revenue. The Company recognized the proceeds received from HCR as a liability that is being amortized using the effective interest method over the life of the arrangement. At the transaction date, the Company recorded the net proceeds of $44.8 million as a liability. In order to determine the amortization of the liability, the Company is required to estimate the total amount of future net royalty payments to be made to HCR over the term of the Royalty Agreement. The total threshold of net royalties to be paid, less the net proceeds received, will be recorded as interest expense over the life of the liability. The Company imputes interest on the unamortized portion of the liability using the effective interest method. The annual effective interest rate as of December 31, 2021 was 18.3% which is reflected as interest expense in the consolidated statements of operations and comprehensive loss. Over the course of the Royalty Agreement, the actual interest rate will be

affected by the amount and timing of royalty revenue recognized and changes in forecasted royalty revenue. There are a number of factors that could materially affect the amount and timing of royalty payments from MTPC, none of which are within the Company's control. On a quarterly basis, the Company reassesses the effective interest rate and adjusts the rate prospectively as needed.

The following table shows the activity within the liability account for the year ended December 31, 2021:

	December 31, 2021 (in thousands)
Liability related to sale of future royalties, net — beginning balance	$ —
Proceeds from sale of future royalties, net	44,783
MTPC royalties payable	(821)
Non-cash interest expense recognized	9,117
Liability related to sale of future royalties, net — ending balance	$ 53,079

The Royalty Agreement requires the Company to take certain actions, including actions with respect to the Royalty Interest Payments, the MTPC Agreement, the MTPC Supply Agreement, and the Company's intellectual property. The Royalty Agreement also contains certain representations and warranties, covenants, indemnification obligations, events of default and other provisions that are customary for a royalty monetization transaction of this nature. In addition, the Company granted HCR a precautionary security interest in connection with the Royalty Interest Payments.

6. Available For Sale Securities

Available for sale securities at December 31, 2021 and 2020 consist of the following:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
December 31, 2021				
Cash and cash equivalents	$ 149,800	$ —	$ —	$ 149,800
Total cash, cash equivalents, and available for sale securities	$ 149,800	$ —	$ —	$ 149,800

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
December 31, 2020				
Cash and cash equivalents	$ 228,698	$ —	$ —	$ 228,698
Available for sale securities:				
Certificates of deposit	$ 39,979	$ 13	$ —	$ 39,992
Total available for sale securities	$ 39,979	$ 13	$ —	$ 39,992
Total cash, cash equivalents, and available for sale securities	$ 268,677	$ 13	$ —	$ 268,690

There were no realized gains or losses on available for sale securities for the years ended December 31, 2021 or 2020. Additionally, the Company did not have any available for sale securities that were in an unrealized loss position as of December 31, 2021 or 2020. As such, the Company did not recognize any credit losses during the year ended December 31, 2021.

7. Fair Value of Financial Instruments

The Company utilizes a portfolio management company for the valuation of the majority of its investments. This company is an independent, third-party vendor recognized to be an industry leader with access to market information that obtains or computes

fair market values from quoted market prices, pricing for similar securities, recently executed transactions, cash flow models with yield curves and other pricing models. For valuations obtained from the pricing service, the Company performs due diligence to understand how the valuation was calculated or derived, focusing on the valuation technique used and the nature of the inputs.

Based on the fair value hierarchy, the Company classifies its cash equivalents and available for sale securities within Level 1 or Level 2. This is because the Company values its cash equivalents and available for sale securities using quoted market prices or alternative pricing sources and models utilizing market observable inputs.

Assets measured or disclosed at fair value on a recurring basis as of December 31, 2021 and 2020 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
December 31, 2021				
Assets:				
Cash and cash equivalents	$ 149,800	—	—	$ 149,800
	$ 149,800	$ —	$ —	$ 149,800
Liabilities:				
Derivative liability	—	—	$ 1,820	$ 1,820
	$ —	$ —	$ 1,820	$ 1,820

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
December 31, 2020				
Assets:				
Cash and cash equivalents	$ 228,698	—	—	$ 228,698
U.S. government debt securities	—	39,992	—	39,992
	$ 228,698	$ 39,992	$ —	$ 268,690
Liabilities:				
Derivative liability	—	—	$ 2,420	$ 2,420
	$ —	$ —	$ 2,420	$ 2,420

The Company's Loan Agreement with Pharmakon (see Note 11) contains certain provisions that change the underlying cash flows of the debt instrument, including a potential extension to the interest-only period dependent on both (a) no event of default having occurred and continuing and (b) the Company achieving certain regulatory and revenue conditions. The Company also assessed the acceleration of the obligations under the Loan Agreement under an event of default. In addition, under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. In accordance with ASC 815, the Company concluded that these features are not clearly and closely related to the host instrument, and represent a single compound derivative that is required to be re-measured at fair value on a quarterly basis.

The events of default include maintaining, on an annual basis, a minimum liquidity threshold which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. The Company recorded a derivative liability related to the Company's Loan Agreement with Pharmakon of $1.8 million and $2.4 million as of December 31, 2021 and 2020, respectively. The Company classified the derivative liability as a non-current liability on the balance sheet at December 31, 2021 and 2020. The estimated fair value of the derivative liability on both December 31, 2021 and 2020 was determined using a scenario-based approach and discounted cash flow model that includes principal and interest payments under various scenarios involving clinical development success for vadadustat and various cash flow assumptions. Probabilities surrounding clinical development success were derived using industry benchmarks. Should the Company's

assessment of the probabilities around these scenarios change, including for changes in market conditions, there could be a change to the fair value of the derivative liability.

The following table provides a roll-forward of the fair value of the derivative liability (in thousands):

Balance at December 31, 2020	$ 2,420
Change in fair value of derivative liability, recorded as other income	(600)
Balance at December 31, 2021	$ 1,820

The Company had no other assets or liabilities measured at fair value on a recurring basis using significant unobservable inputs (Level 3) at December 31, 2021 and 2020.

Investment securities are exposed to various risks such as interest rate, market and credit risks. When the Company holds investment securities, due to the level of risk associated with certain investment securities and the level of uncertainty related to changes in the value of investment securities, the Company considers if changes in risks in the near term would result in material changes in the fair value of investments.

8. Inventory

The components of inventory are summarized as follows:

	December 31, 2021	December 31, 2020
	(in thousands)	
Raw materials	$ 1,763	$ 2,542
Work in process	62,635	64,076
Finished goods	14,661	19,691
Total inventory	$ 79,059	$ 86,309

Long-term inventory, which primarily consists of raw materials and work in process, is included in other assets in the Company's consolidated balance sheets.

	December 31, 2021	December 31, 2020
	(in thousands)	
Balance Sheet Classification:		
Inventory	$ 38,195	$ 61,017
Other assets	40,864	25,292
Total inventory	$ 79,059	$ 86,309

Inventory amounts written down as a result of excess, obsolescence, scrap or other reasons and charged to cost of goods sold totaled $15.6 million, $20.1 million, and $7.1 million during the years ended December 31, 2021, 2020, and 2019 respectively. The decrease in inventory amounts written down for the year ended December 31, 2021 as compared to the year ended December 31, 2020 was primarily due to lower write-downs to inventory reserves related to a previously disclosed manufacturing quality issue related to Auryxia during 2020. In addition, there were $8.7 million, $11.4 million, and $17.1 million in related step-up charges during the years ended December 31, 2021, 2020, and 2019, respectively. During the fourth quarter of 2021, the Company recorded $12.5 million of receipts related to inventory previously identified as excess as a reduction to the excess purchase commitment liability.

If future sales of Auryxia are lower than expected, the Company may be required to write-down the value of such inventories. Inventory write-downs and losses on purchase commitments are recorded as a component of cost of sales in the consolidated statement of operations.

9. Intangible Assets and Goodwill

Intangible Assets

The following table presents the Company's intangible assets (in thousands):

	December 31, 2021			
	Gross Carrying Value	Accumulated Amortization	ASC 842 Adjustment	Total
Acquired intangible assets:				
Developed product rights for Auryxia	213,603	(105,476)	—	108,127
Total	$ 213,603	$ (105,476)	$ —	$ 108,127

	December 31, 2020			
	Gross Carrying Value	Accumulated Amortization	ASC 842 Adjustment	Total
Acquired intangible assets:				
Developed product rights for Auryxia	$ 213,603	$ (69,433)	$ —	$ 144,170
Favorable lease	545	(5)	(540)	—
Total	$ 214,148	$ (69,438)	$ (540)	$ 144,170

On December 12, 2018, the Company completed the Merger, whereby it acquired certain definite-lived intangible assets, including the developed product rights for Auryxia and a favorable lease. The Company amortizes its definite-lived intangible assets acquired as part of the Merger using the straight-line method, which is considered the best estimate of economic benefit, over its estimated useful life of six years. As a result of the adoption of ASC 842 on January 1, 2019, the Company reclassed the remaining balance of the favorable lease intangible asset into the operating lease asset. The Company recorded $36.0 million, $31.5 million and $36.4 million in amortization expense related to the developed product rights for Auryxia during the years ended December 31, 2021, 2020 and 2019, respectively. Estimated future amortization expense for the intangible asset as of December 31, 2021 is as follows (in thousands):

	Total
2022	$ 36,043
2023	36,042
2024	36,042
2025	—
2026	—
Thereafter	—
	$ 108,127

Auryxia Intangible Asset Impairment

In the second quarter of 2020, in connection with a routine business review, the Company reduced its short-term and long-term Auryxia revenue forecast. This reduction was primarily driven by the compounding impact of the September 2018 CMS decision that rescinded Medicare Part D coverage of Auryxia for the IDA Indication and the related imposition by CMS of a prior authorization requirement for Auryxia for the Hyperphosphatemia Indication. As a result, the Company determined indicators of impairment existed for the developed product rights for Auryxia and performed an undiscounted cash flow analysis pursuant to ASC 360-10, *Impairment or Disposal of Long-lived Assets*, to determine if the cash flows expected to be generated by the Auryxia asset group over the estimated remaining useful life of the primary assets were sufficient to recover the carrying value of the Auryxia asset group. Based on this analysis, the undiscounted cash flows were not sufficient to recover the carrying value of the Auryxia asset group. As a result, the Company was required to perform Step 3 of the impairment test to determine the fair value of the Auryxia asset group.

To estimate the fair value, the Company performed a business enterprise valuation for the Auryxia asset group using the income approach, which is based on a discounted cash flow analysis and calculates the fair value by estimating the after-tax cash flows attributable to the asset group and then discounting the after-tax cash flows to present value using a risk-adjusted discount rate. Key estimates and assumptions used in the valuations included projected revenues and expenses related to the asset, estimated contributory asset charges, and a risk-adjusted discount rate of 9.5% to calculate the present value of the future expected cash inflows. The Company believes its assumptions are consistent with the plans and estimates that a market participant would use

to manage the business. The discount rates used are intended to reflect the risks inherent in future cash flow projections and were based on an estimate of the weighted average cost of capital, or WACC, of market participants relative to the Auryxia asset group.

As a result of this analysis, the fair value of the Auryxia asset group was below its carrying value, and the Company recorded an impairment charge of $115.5 million during the three months ended June 30, 2020 and made a corresponding adjustment to the estimated useful life of the developed product rights for Auryxia from nine years to seven years. The impairment charge has been entirely allocated to the Company's only intangible asset, the developed product rights for Auryxia, as all other long-lived assets had fair values that were either equal to or greater than their carrying value. Per ASC 360-10, the carrying amount of a long-lived asset of the group would not be reduced below its fair value. The Company believes its assumptions used to determine the fair value of the Auryxia asset group are reasonable. In the event the estimates and assumptions used in the valuation of the Auryxia asset group, including the forecasted projections, change in the future, additional impairment charges could be recorded in the future.

In the fourth quarter of 2020, as part of the Company's routine forecasting process, the Company reassessed and prospectively adjusted the estimated useful life of the developed product rights for Auryxia from seven years to six years. This was not deemed an impairment indicator as of December 31, 2020.

Goodwill

Goodwill was $55.1 million as of December 31, 2021 and 2020, derived as follows (in thousands):

Total Merger consideration	$	527,754
Less: Fair value of identified acquired assets and liabilities, net		(472,701)
Goodwill	$	55,053

The Company operates in one operating segment which the Company considers to be the only reporting unit. Goodwill is evaluated for impairment at the reporting unit level on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that an impairment may exist. There were no impairments of goodwill during the years ended December 31, 2021, 2020 and 2019.

10. Accrued Expenses

Accrued expenses are as follows:

	December 31, 2021	December 31, 2020
	(in thousands)	
Product revenue allowances	$ 26,624	$ 38,049
Accrued clinical	14,036	28,986
Amounts due to collaboration partners	22,654	17,977
Otsuka PRV contribution	—	10,000
Accrued payroll and related	15,863	14,899
Lease liability	4,802	5,286
Royalties	3,472	2,998
Professional fees	1,899	3,271
Accrued commercial manufacturing	3,843	514
Accrued other	11,263	8,644
Total accrued expenses	$ 104,456	$ 130,624

11. Debt

Future principal payments pursuant to the contractual terms of the Term Loans (as defined below) as of December 31, 2021 are as follows (in thousands):

	Principal Payments (in thousands)
2022	$ 7,140
2023	33,474
2024	59,386
2025	—
2026	—
Thereafter	—
Total before unamortized discount and issuance costs	100,000
Less: unamortized discount and issuance costs	(2,457)
Total term loans	$ 97,543

Term Loans

On November 11, 2019, the Company, with Keryx as guarantor, entered into a loan agreement, or the Loan Agreement, with BioPharma Credit PLC as collateral agent and a lender, or the Collateral Agent, and BioPharma Credit Investments V (Master) LP as a lender, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to the Company in two tranches, subject to certain terms and conditions, or the Term Loans. BioPharma Credit PLC subsequently transferred its interest in the Term Loans, solely in its capacity as a lender, to its affiliate, BPCR Limited Partnership. The Collateral Agent and the lenders are collectively referred to as Pharmakon. The first tranche of $80.0 million, or Tranche A, was drawn on November 25, 2019, or the Tranche A Funding Date, and the second tranche of $20.0 million, or Tranche B, was drawn on December 10, 2020, or the Tranche B Funding Date. Each of the Tranche A Funding Date and the Tranche B Funding Date, a Funding Date.

Proceeds from the Term Loans may be used for general corporate purposes. The Company and Keryx entered into a Guaranty and Security Agreement with the Collateral Agent, or the Guaranty and Security Agreement, on the Tranche A Funding Date. Pursuant to the Guaranty and Security Agreement, the Company's obligations under the Term Loans are unconditionally guaranteed by Keryx, or the Guarantee. Additionally, the obligations of the Company and Keryx under the Term Loans and the Guarantee are secured by a first priority lien on certain assets of the Company and Keryx, including Auryxia and certain related assets, cash, and certain equity interests held by the Company and Keryx, collectively the Collateral.

The Term Loans bear interest at a floating rate per annum equal to the three-month LIBOR rate plus 7.50%, subject to a 2.00% LIBOR floor and a 3.35% LIBOR cap, payable quarterly in arrears. The Term Loans will mature on the fifth anniversary of the Tranche A Funding Date, or the Maturity Date. The Company will repay the principal under the Term Loans in equal quarterly payments starting on the 33rd-month anniversary of the applicable Funding Date or, if certain conditions are met, it will have the option to repay the principal in equal quarterly payments starting on the 48th-month anniversary of the applicable Funding Date, or collectively the Amortization Schedule. Under certain circumstances, unless certain liquidity conditions are met, the Maturity Date may decrease by up to one year, and the Amortization Schedule may correspondingly commence up to one year earlier.

On the Tranche A Funding Date, the Company paid to Pharmakon a facility fee equal to 2.00% of the aggregate principal amount of the Term Loans, or $2.0 million, in addition to other expenses incurred by Pharmakon and reimbursed by the Company, or Lender Expenses. The Tranche A draw was $77.3 million, net of facility fee, Lender Expenses and issuance costs. The Tranche B draw was $20.0 million, net of immaterial Lender Expenses and issuance costs. The Loan Agreement permits voluntary prepayment at any time in whole or in part, subject to a prepayment premium. The prepayment premium would be 2.00% of the principal amount being prepaid prior to the third anniversary of the applicable Funding Date, 1.00% on or after the third anniversary, but prior to the fourth anniversary, of the applicable Funding Date, and 0.50% on or after the fourth anniversary of the applicable Funding Date but prior to the Maturity Date, and a make-whole premium on or prior to the second anniversary of the applicable Funding Date in an amount equal to foregone interest through the second anniversary of the applicable Funding Date. A change of control triggers a mandatory prepayment of the Term Loans.

The Loan Agreement contains customary representations, warranties, events of default and covenants of the Company and its subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. On February 18, 2022, the Loan Agreement was amended, which waived the provision under the Loan Agreement that required the Company to not be subject to any qualification as a going concern within the Company's 2021 Annual Report on Form 10-K. Pursuant to the Loan Agreement, as amended, the Company's filings of Form 10-Q for fiscal quarters ending June 30, 2022 and September 30, 2022, and its future Annual Reports on Form 10-K, must not be subject to any qualification as to going concern. If the Company does not satisfy the covenant as to going concern in any of these filings, the Company will be in default under the Loan Agreement. There is uncertainty as to whether or not the Company will meet our future quarterly and annual debt covenants related to qualification as to going concern. If an event of default occurs and is continuing under the Loan Agreement, the Collateral Agent is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement. Therefore, as of December 31, 2021, the Company classified the borrowings under the Loan Agreement as current. Under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. As of December 31, 2021, the Company determined that no events of default had occurred.

The Company assessed the terms and features of the Loan Agreement in order to identify any potential embedded features that would require bifurcation or any beneficial conversion feature. As part of this analysis, the Company assessed the economic characteristics and risks of the Loan Agreement, including put and call features. The terms and features assessed include a potential extension to the interest-only period dependent on both no event of default having occurred and continuing and on the Company achieving certain regulatory and revenue conditions. The Company also assessed the acceleration of the obligations under the Loan Agreement under an event of default. In addition, under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. In accordance with ASC 815, the Company concluded that these features are not clearly and closely related to the host instrument, and represent a single compound derivative that is required to be re-measured at fair value on a quarterly basis.

The fair value of the derivative liability related to the Company's Loan Agreement was $1.8 million and $2.4 million as of December 31, 2021 and 2020, respectively. The Company classified the derivative liability as a non-current liability on the balance sheet at December 31, 2021.

The Company recognized approximately $10.9 million and $8.9 million of interest expense related to the Loan Agreement during the years ended December 31, 2021 and 2020, respectively.

12. Warrant

In connection with the Janssen Agreement, in February 2017, the Company issued a warrant to purchase 509,611 shares of the Company's common stock at an exercise price of $9.81 per share. The warrant was fully vested upon issuance and exercisable in whole or in part, at any time prior to February 9, 2022. The warrant satisfied the equity classification criteria of ASC 815, and is therefore classified as an equity instrument. The fair value at issuance of $3.4 million was calculated using the Black-Scholes option pricing model and was charged to research and development expense as it represented consideration for a license for which the underlying intellectual property was deemed to have no alternative future use. As of December 31, 2021, the warrant remained outstanding. The Warrant expired on February 9, 2022.

13. Stockholders' Equity

Authorized and Outstanding Capital Stock

On June 5, 2020, the Company filed a Certificate of Amendment to its Ninth Amended and Restated Certificate of Incorporation, or its Charter, to increase the number of authorized shares of common stock from 175,000,000 to 350,000,000. As of December 31, 2021, the authorized capital stock of the Company included 350,000,000 shares of common stock, par value $0.00001 per share, of which 177,000,963 and 148,074,085 shares were issued and outstanding at December 31, 2021 and 2020, respectively; and 25,000,000 shares of undesignated preferred stock, par value $0.00001 per share, of which no shares were issued and outstanding at December 31, 2021 and 2020.

At-the-Market Facility

On November 12, 2019, the Company entered into an Amended and Restated Controlled Equity Offering℠ Sales Agreement with Cantor Fitzgerald & Co. for the offer and sale of common stock at the then current market prices in amounts to be determined from time to time. Also, on November 12, 2019, the Company filed a prospectus supplement pursuant to which it was able to offer and sell up to $75.0 million of its common stock at the then current market prices from time to time. In

December 2019, the Company commenced sales under this program. Through December 31, 2019, the Company sold 2,684,392 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $16.8 million. During the three months ended March 31, 2020, the Company sold 7,973,967 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $56.7 million.

On March 12, 2020, the Company filed an additional prospectus supplement, pursuant to which it is able to offer and sell up to $65.0 million of its common stock at current market prices from time to time. During the year ended December 31, 2020, the Company sold 3,509,381 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $10.6 million. During the three months ended March 31, 2021, the Company sold 5,224,278 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $15.9 million.

On February 25, 2021, the Company filed a prospectus relating to the sales agreement with its new shelf registration statement (which replaced the prior shelf registration statement and the sales agreement prospectus supplement), pursuant to which it is able to offer and sell up to $100.0 million of its common stock at current market prices from time to time. During the year ended December 31, 2021 and through the date of this Annual Report on Form 10-K, the Company sold 21,532,665 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $73.2 million.

Equity Offering

In May 2020, the Company sold 12,650,000 shares of its common stock in a public offering at a price of $12.00 per share, including 1,650,000 shares from the full exercise of the underwriters' option to purchase additional shares. The aggregate net proceeds received by the Company from the offering were $142.4 million, net of underwriting discounts and commissions and offering expenses payable by the Company.

Equity Plans

On February 28, 2014, the Company's Board of Directors adopted its 2014 Incentive Plan and its 2014 Employee Stock Purchase Plan, or the 2014 ESPP, which were subsequently approved by its shareholders and became effective upon the closing of the Company's initial public offering on March 25, 2014. The Company's 2014 Incentive Plan was subsequently amended on December 11, 2018, which amendment did not require shareholder approval. The Company's 2014 Incentive Plan, as amended, is referred to as the 2014 Plan. The 2014 Plan replaced the Company's Amended and Restated 2008 Equity Incentive Plan, or the 2008 Plan; however, options or other awards granted under the 2008 Plan prior to the adoption of the 2014 Plan that have not been settled or forfeited remain outstanding and effective. On June 6, 2019, the Company's shareholders approved the Amended and Restated 2014 Employee Stock Purchase Plan, or the ESPP. In May 2016, the Company's Board of Directors approved an inducement award program that was separate from the Company's equity plans and which, consistent with Nasdaq Listing Rule 5635(c)(4), did not require shareholder approval, or the Inducement Award Program. During the year ended December 31, 2021, the Company granted 1,373,200 options to purchase shares of the Company's common stock to new hires under the Inducement Award Program, of which 1,238,200 options to purchase shares of the Company's common stock remained outstanding at December 31, 2021.

The 2014 Plan allows for the granting of stock options, stock appreciation rights, or SARs, restricted stock, unrestricted stock, RSUs, performance awards and other awards convertible into or otherwise based on shares of the Company's common stock. Dividend equivalents may also be provided in connection with an award under the 2014 Plan. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2014 Plan. The Company initially reserved 1,785,000 shares of its common stock for the issuance of awards under the 2014 Plan. The 2014 Plan provides that the number of shares reserved and available for issuance under the 2014 Plan will automatically increase annually on January 1 of each calendar year, by an amount equal to three percent (3%) of the number of the Company's shares outstanding on a fully diluted basis as of the close of business on the immediately preceding December 31, or the 2014 Plan Evergreen Provision. The Company's Board of Directors may act prior to January 1 of any year to provide that there will be no automatic increase in the number of Akebia Shares available for grant under the 2014 Plan for that year (or that the increase will be less than the amount that would otherwise have automatically been made). On December 12, 2018, in connection with the consummation of the Merger, the Company assumed outstanding and unexercised options to purchase Keryx Shares, as adjusted by the Exchange Multiplier pursuant to the terms of the Merger Agreement, under the following Keryx equity plans, or the Keryx Equity Plans: the Keryx 1999 Share Option Plan, the Keryx 2004 Long-Term Incentive Plan, the Keryx 2007 Incentive Plan, the Keryx Amended and Restated 2013 Incentive Plan, and the Keryx 2018 Equity Incentive Plan, or the Keryx 2018 Plan. In addition, the number of Keryx Shares available for issuance under the Keryx 2018 Plan, as adjusted by the Exchange Multiplier pursuant to the terms of the Merger Agreement, may be used for awards granted by the Company under its 2014 Plan, or the Assumed

Shares, provided that the Company uses the Assumed Shares for individuals who were not employees or directors of the Company prior to the consummation of the Merger. During the year ended December 31, 2021, the Company granted 1,997,200 options to purchase Akebia Shares to employees under the 2014 Plan, 1,373,200 options to purchase Akebia Shares to employees under the Inducement Award Program, 3,399,412 Akebia RSUs to employees under the 2014 Plan, 136,708 Akebia PSUs to employees under the 2014 Plan, 281,000 options to purchase Akebia Shares to directors under the 2014 Plan, and 82,200 Akebia RSUs to directors under the 2014 Plan.

The ESPP provides for the issuance shares of the Company's common stock to participating employees at a discount to their fair market value. As noted above, the Company's stockholders approved the ESPP, which amended and restated the Company's 2014 ESPP, on June 6, 2019. The maximum aggregate number of shares at December 31, 2021 of the Company's common stock available for future issuance under the ESPP is 5,173,141. Under the ESPP, each offering period is six months, at the end of which employees may purchase shares of the Company's common stock through payroll deductions made over the term of the offering. The per-share purchase price at the end of each offering period is equal to the lesser of eighty-five percent (85%) of the closing price of the Company's common stock at the beginning or end of the offering period.

Shares Reserved for Future Issuance

The Company has reserved for future issuance the following number of shares of common stock:

	December 31, 2021	December 31, 2020
Common stock options, RSUs and PSUs outstanding (1)	16,065,218	14,108,828
Shares available for issuance under Akebia equity plans (2)	4,675,734	3,468,080
Warrant to purchase common stock	509,611	509,611
Shares available for issuance under the ESPP	5,173,141	5,480,334
Total	26,423,704	23,566,853

(1) Includes awards granted under the 2014 Plan and the Inducement Award Program and awards issued in connection with the Merger.
(2) On January 1, 2022, January 1, 2021 and January 1, 2020, the shares reserved for future grants under the 2014 Plan increased by 5,807,270, 4,880,775 and 4,031,376 shares, respectively, pursuant to the 2014 Plan Evergreen Provision.

Stock-Based Compensation

Stock Options

Service-Based Stock Options

On February 28, 2021, as part of the Company's annual grant of equity, the Company issued 1,997,200 stock options to employees. In addition, the Company issues stock options to directors, new hires and occasionally to other employees not in connection with the annual grant process. Options granted by the Company vest over periods of between 12 and 48 months, subject, in each case, to the individual's continued service through the applicable vesting date. Options vest either 100% on the first anniversary of the grant date or in installments of (i) 25% at the one year anniversary and (ii) 12 equal quarterly installments beginning after the one year anniversary of the grant date, subject to the individual's continuous service with the Company. Options generally expire ten years after the date of grant. The Company recorded approximately $8.9 million, $8.5 million and $5.4 million of stock-based compensation expense related to stock options granted during the years ended December 31, 2021, 2020 and 2019, respectively.

The assumptions used in the Black-Scholes pricing model to estimate the grant date fair value of options granted under the 2014 Plan are as follows:

	Year ended December 31,								
	2021			2020			2019		
Risk-free interest rate	0.66%	-	1.37%	0.32%	-	1.38%	1.42%	-	2.57%
Dividend yield		—%			—%			—%	
Volatility	77.81%	-	81.79%	69.56%	-	75.91%	61.4%	-	64.1%
Expected term (years)	5.51	-	6.25	5.51	-	6.25	5.51	-	6.25

The following table summarizes the Company's stock option activity, excluding performance-based options, for the year ended December 31, 2021:

	Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2020	9,370,373	$ 9.31		$ 387,596
Granted	3,651,400	$ 3.34		
Exercised	—	$ —		$ —
Forfeited	(1,517,165)	$ 7.70		$ 43,756
Expired/cancelled	(106,393)	$ 11.35		
Outstanding, December 31, 2021	11,398,215	$ 7.60	7.24	$ 267,830
Options exercisable, December 31, 2021	5,848,562	$ 9.92	5.80	$ 267,440
Vested and expected to vest, December 31, 2021	11,398,215	$ 7.60		

The weighted-average grant date fair values of options granted in the years ended December 31, 2021, 2020, and 2019 were $2.29, $5.63, and $3.85 per share, respectively. There was no intrinsic value of options exercised during the year ended December 31, 2021, as there were no options exercised in 2021. The total intrinsic value of options exercised during the years ended December 31, 2020 and 2019 were $0.4 million and $1.3 million, respectively. The fair value of options that vested during the years ended December 31, 2021, 2020, and 2019 were $10.6 million, $6.8 million, and $4.3 million, respectively. As of December 31, 2021, there was approximately $15.7 million of unrecognized compensation cost related to stock options outstanding under the Company's 2014 Plan or made pursuant to the Inducement Award Program, which is expected to be recognized over a weighted average period of 2.33 years.

Performance-Based Stock Options

The Company also grants performance-based stock options to employees under the 2014 Plan. The performance-based stock options granted by the Company vest in connection with the achievement of specified commercial and regulatory milestones. The performance-based stock option also feature a time-based vesting component. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of options granted and recognized over time based on the probability of meeting such commercial and regulatory milestones. The Company issued 99,558 and no performance-based options during the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, the Company had 99,558 performance-based options outstanding compared to no performance-based options outstanding at December 31, 2020.

The following table summarizes the Company's performance-based option activity for the year ended December 31, 2021:

	Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2020	—	$ —		$ —
Granted	99,558	$ 2.74		
Exercised	—	$ —		$ —
Forfeited/cancelled		$ —		
Outstanding, December 31, 2021	99,558	$ 2.74	9.6	$ —

The Company did not record any stock-based compensation expense related to performance-based options during 2021, 2020 and 2019. There were no performance-based options that vested during fiscal year 2021 or 2020, and 46,790 performance-based options that vested during fiscal year 2019. As of December 31, 2021, there were no unrecognized compensation costs related to performance-based stock options under the Company's 2014 Plan.

Restricted Stock Units

Service-Based Restricted Stock Units

On February 28, 2021, as part of the Company's annual grant of equity, the Company issued 3,180,400 restricted stock units, or RSUs, to employees. In addition, the Company occasionally issues RSUs not in connection with the annual grant process to employees. Generally, RSUs granted by the Company vest in one of the following ways: (i) 100% of each RSU grant vests on either the first or the third anniversary of the grant date, (ii) one third of each RSU grant vests on the first, second and third anniversaries of the grant date, subject, in each case, to the individual's continued service through the applicable vesting date, or

(iii) 50% of each RSU grant vests on the first anniversary and 25% of each RSU grant vests every six months after the one year anniversary of the grant date. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of units granted and recognized on a straight-line basis over the vesting period. The Company recorded approximately $12.9 million, $14.6 million and $6.2 million of stock-based compensation expense related to employee RSUs in 2021, 2020 and 2019, respectively.

On December 12, 2018, pursuant to the Merger Agreement, each Keryx Share that was subject to a Keryx restricted share award, other than those Keryx restricted shares that accelerated or lapsed as a result of the completion of the Merger, was converted into an RSU award of Akebia, covering the number of Akebia Shares determined in accordance with the Exchange Multiplier. As a result, the Company issued 486,709 service-based RSUs in substitution for Keryx restricted share awards in connection with the Merger. These RSUs vest either (i) in 3 equal annual installments beginning after the one year anniversary of the grant date or (ii) one third on the one year anniversary of the grant date with the remaining RSUs vesting on the first day of each calendar quarter over the next two years thereafter. As of October 1, 2021, the RSU awards granted in connection with the Merger were fully vested and none are outstanding as of December 31, 2021.

Performance-Based Restricted Stock Units

During the year ended December 31, 2021, the Company issued 37,150 performance-based restricted stock units, or PSUs, to the Company's executives. The PSUs granted by the Company vest in connection with the achievement of specified commercial and regulatory milestones. The PSUs also feature a time-based vesting component. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of units granted and recognized over time based on the probability of meeting such commercial and regulatory milestones. The Company recorded approximately $0.3 million, $0.5 million and $0 of stock-based compensation expense related to employee PSUs in 2021, 2020 and 2019, respectively.

The following table summarizes the Company's RSU and PSU activity for the year ended December 31, 2021:

	Shares		Weighted-Average Grant Date Fair Value
Unvested balance, December 31, 2020	4,725,353	$	7.43
Granted	3,518,762	$	3.44
Vested	(2,267,342)	$	6.77
Forfeited	(1,422,430)	$	5.82
Unvested balance, December 31, 2021	4,554,343	$	5.17

The total fair value of RSUs and PSUs that vested during 2021, 2020 and 2019 (measured on the date of vesting) was $15.4 million, $9.4 million, and $2.7 million, respectively. As of December 31, 2021, there was approximately $12.4 million of unrecognized compensation cost related to RSUs and PSUs, which is expected to be recognized over a weighted average period of 1.56 years.

There are 13,102 performance-based RSUs, issued in connection with the Merger, outstanding at December 31, 2021.

Employee Stock Purchase Plan

The first offering period under the ESPP opened on January 2, 2015. The Company issued 307,193 shares during the year ended December 31, 2021. The Company recorded approximately $0.6 million, $0.8 million and $0.3 million of stock-based compensation expense related to the ESPP during 2021, 2020 and 2019, respectively.

Compensation Expense Summary

The Company has classified its stock-based compensation expense related to share-based awards as follows:

	Years ended December 31,		
	2021	2020	2019
	(in thousands)		
Research and development	$ 5,816	$ 6,113	$ 3,544
Selling, general and administrative	16,919	18,347	8,381
Total	$ 22,735	$ 24,460	$ 11,925

Compensation expense by type of award:

	Years ended December 31,		
	2021	2020	2019
	(in thousands)		
Stock options	$ 8,958	$ 8,517	$ 5,421
Restricted stock units	12,927	14,639	6,240
Performance RSUs	294	464	—
Employee stock purchase plan	556	840	264
Total	$ 22,735	$ 24,460	$ 11,925

14. Income Taxes

The Company's income tax provision was computed based on the federal statutory rate and the state statutory rates, net of the related federal benefit. At December 31, 2018 the Company recorded a tax benefit of $28.3 million as a result of the Merger with Keryx. As part of purchase accounting, the Company recorded a deferred tax liability that is a source of income for which the Company can benefit from its tax attributes. The use of the Company's tax attributes resulted in a release of the corresponding valuation allowance associated with this benefit. At December 31, 2019 the Company recorded an additional tax benefit of $6.6 million as a result of additional losses incurred during the year. There was no current or deferred income tax expense or benefit for the years ended December 31, 2021 and December 31, 2020 due to the Company's net losses and increases in its valuation allowance against its deferred tax assets.

The provision for income taxes for each of the years ended December 31, 2021, 2020 and 2019 consisted of the following:

	Year ended December 31,		
	2021	2020	2019
Current:			
Federal	—	—	—
State	—	—	—
Foreign	—	—	—
Total Current:	—	—	—
Deferred:			
Federal	—	—	—
State	—	—	(6,631)
Foreign	—	—	—
Total Deferred:	—	—	(6,631)
Total Income Taxes	—	—	(6,631)

Our effective income tax rate differs from the statutory federal income tax rate as follows for the years ended December 31, 2021, 2020 and 2019:

	Year ended December 31,		
	2021	2020	2019
Federal tax at statutory rate	21.0 %	21.0 %	21.0 %
State and local tax at statutory rate	3.0	3.0	5.5
Research and development tax credits	—	0.1	2.0
Change in valuation allowance	(22.7)	(21.5)	(22.4)
Other permanent differences	(1.0)	(0.4)	(0.3)
Reduction in deferred tax assets for change in ownership	—	—	(1.6)
Effect of rate changes	0.3	0.8	(1.4)
Provision to Return Adjustment	0.3	(1.5)	—
Prior Period Adjustment to State NOL DTA	—	(1.5)	—
Other	(0.9)	—	(0.5)
Effective tax rate	— %	— %	2.3 %

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. When realization of the deferred tax asset is more likely than not to occur, the benefit related to the deductible temporary differences attributable to operations is recognized as a reduction of income tax expense. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized. The Company cannot be certain that future taxable income will be sufficient to realize its deferred tax assets. Accordingly, the Company has recorded a valuation allowance against the Company's otherwise recognizable net deferred tax assets. The Company continues to maintain the underlying tax benefits to offset future taxable income and to monitor the need for a valuation allowance based on the profitability of its future operations. The valuation allowance increased by approximately $64.2 million and $82.5 million, during the years ended December 31, 2021 and 2020, respectively. Significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31,	
	2021	2020
	(in thousands)	
Deferred tax assets:		
Accrued expenses	$ 3,306	$ 3,079
Deferred revenue	9,725	9,091
Sale of Royalty	12,037	—
Stock based compensation	9,194	10,014
Research and development credits	5,034	4,620
Other non-current liabilities	20,424	17,015
Net operating loss carryforward	286,908	262,532
ASC 842 lease liability	9,096	6,776
Fixed assets	799	700
UNICAP	3,190	2,132
Inventory Reserve	10,281	8,260
Derivative Liability	413	542
Other	6,081	2,535
Total deferred tax assets	376,488	327,296
Less valuation allowance	(342,122)	(277,941)
Total deferred tax assets, net of valuation allowance	34,366	49,355
Deferred tax liabilities:		
Fixed assets	—	—
Intangible assets	(25,598)	(34,178)
Inventory	—	(8,479)
ASC 842 ROU asset	(8,486)	(6,101)
Other	(282)	(597)
Total deferred tax liabilities	(34,366)	(49,355)
Net deferred tax liability	$ —	$ —

At December 31, 2021 and 2020, the Company has approximately $0.3 million (after amortization of $1.7 million) and $0.4 million (after amortization of $1.6 million), respectively, of start-up expenses capitalized for income tax purposes with amortization available to offset future federal, state and local income tax.

As of December 31, 2021 and 2020, the Company has approximately $1,223.3 million and $1,128.3 million, respectively, of federal NOL carry-forwards which expire through 2037. Included in the $1,223.3 million of federal NOLs are losses of $641.4 million that will carry forward indefinitely as a result of the Tax Cuts and Jobs Act. Additionally, at December 31, 2021 and 2020, the Company has approximately $1,792.1 million and $1,620.7 million, respectively, of state NOL carry-forwards which expired through 2041. The Company also has approximately $2.5 million of federal research and development tax credit carryforwards which expire through 2040 and $3.2 million of state research and development tax credit carryforwards which expire through 2036.

Under the provisions of the Internal Revenue Code, the net operating losses and tax credit carry-forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating losses and tax credit carryforwards may become subject to an annual limitation under Internal Revenue Code 382 and 383 if there is more than a 50% change in ownership of the stockholders that own 5% or more of the Company's outstanding stock over a three-year period. The Company completed an evaluation of its ownership changes and concluded that an ownership change did occur on December 12, 2018 for both Akebia and Keryx in connection with the Merger. As a consequence of this ownership change, the Company's NOLs and tax credit carryforwards allocable to the tax periods preceding the ownership change became subject to limitation under Section 382. The Company reduced its associated deferred tax assets by $44.9 million as a result of the limitation.

The Company files income tax returns in the U.S. federal and various state and local jurisdictions. For federal and state income tax purposes, the 2020, 2019 and 2018 tax years remain open for examination under the normal three-year statute of limitations.

The statute of limitations for income tax audits in the United States will commence upon utilization of net operating losses and will expire three years from the filing of the tax return the loss was utilized on.

There was no accrual for uncertain tax positions or for interest and penalties related to uncertain tax positions for 2021, 2020 and 2019. The Company does not believe that there will be a material change in its unrecognized tax positions over the next twelve months. All of the unrecognized tax benefits, if recognized, would be offset by the valuation allowance.

15. Employee Retirement Plan

In 2008, the Company established a retirement plan, or the Plan, authorized by Section 401(k) of the Internal Revenue Code. In accordance with the Plan, all employees who have attained the age of 21 are eligible to participate in the Plan as of the first Entry Date, as defined, following their date of employment. Each employee can contribute a percentage of compensation up to a maximum of the statutory limits per year. Company contributions are discretionary and contributions in the amount of approximately $1.8 million, $1.6 million and $1.3 million were made during the years ended December 31, 2021, 2020 and 2019, respectively.

16. Commitments and Contingencies

Leases

The Company leases approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts under a lease which was most recently amended in November 2020, collectively the Cambridge Lease. Under the Third Amendment to the Cambridge Lease, or the Third Amendment, executed in July 2016, total monthly lease payments under the initial base rent were approximately $242,000 and are subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises commenced on January 1, 2017 in the monthly amount of approximately $22,000. The Fourth Amendment to the Cambridge Lease, executed in May 2017, provided additional storage space to the Company and did not impact rent payments. In April 2018, the Company entered into a Fifth Amendment to the Cambridge Lease, or the Fifth Amendment, for an additional 19,805 square feet of office space on the 12th floor. Monthly lease payments for the existing 45,362 square feet of office and lab space, under the Third Amendment, remain unchanged. The new space leased by the Company was delivered in September 2018 and additional monthly lease payments of approximately $135,000 commenced in February 2019 and are subject to annual rent escalations, which commenced in September 2019. In November 2020, the Company entered into a Sixth Amendment to the Cambridge Lease, or the Sixth Amendment, to extend the term of the Cambridge Lease with respect to the lab space from November 30, 2021 to January 31, 2025. The Sixth Amendment includes two months of free rent starting in December 2020 and additional monthly lease payments of approximately $48,000, which commenced in December 2021, and is subject to annual rent escalations, which commence in December 2022.

Additionally, as a result of the Merger, the Company has a lease for 27,300 square feet of office space in Boston, Massachusetts, or the Boston Lease, which expires in February 2023. The total monthly lease payments under the base rent are approximately $136,000 and are subject to annual rent escalations. As of the date of the filing of this Annual Report on Form 10-K, the Company has amended the Boston Lease to extend the term as further described in Note 18.

The term of the Cambridge Lease with respect to the office space expires on September 11, 2026, with one five-year extension option available. The term of the Boston Lease office space expires on February 28, 2023, with an extension option for one additional five-year extension option available. The renewal option in the with respect to the Cambridge Lease was not included in the calculation of the operating lease assets and operating lease liabilities as the renewal is not reasonably certain. As of December 31, 2021, the renewal option for the Boston Lease office space was included in the calculation of the operating lease assets and operating lease liabilities as the Company became reasonably certain that the Company would exercise the extension option. As of the date of the filing of this Annual Report on Form 10-K, the Company has amended the Boston Lease to extend the term as further described in Note 18. The term of the Cambridge Lease with respect to the lab space expires on January 31, 2025, with an extension option for one additional period through September 11, 2026. The renewal options in this real estate lease was included in the calculation of the operating lease assets and operating lease liabilities as the renewal is reasonably certain. The lease agreements do not contain residual value guarantees. Operating lease costs were $6.7 million for both the years ended December 31, 2021 and 2020. Cash paid for amounts included in the measurement of operating lease liabilities were $7.1 million and $7.0 million for the years ended December 31, 2021 and 2020, respectively.

In September 2019, Keryx entered into an agreement to sublease the Boston office space to Foundation Medicine, Inc., or Foundation. The sublease is subject and subordinate to the Boston Lease between Keryx and the landlord. The term of the sublease commenced on October 16, 2019, upon receipt of the required consent from the landlord for the sublease agreement, and expires on February 27, 2023. Foundation is obligated to pay Keryx rent that approximates the rent due from Keryx to its

landlord with respect to the Boston Lease. Sublease rental income is recorded to other income. Keryx continues to be obligated for all payment terms pursuant to the Boston Lease, and the Company will guaranty Keryx's obligations under the sublease. Keryx recorded $1.8 million in sublease rental income from Foundation during each of the years ended December 31, 2021 and 2020.

The Company has not entered into any material short-term leases or financing leases as of December 31, 2021.

The total security deposit in connection with the Cambridge Lease is $1.6 million as of December 31, 2021. Additionally, the Company recorded $0.4 million for the security deposit under the Boston Lease. Both the Cambridge Lease and the Boston Lease have their security deposits in the form of a letter of credit, all of which are included as restricted cash in prepaid expenses and other current assets in the Company's consolidated balance sheet as of December 31, 2021.

As of December 31, 2021, undiscounted minimum rental commitments under non-cancelable leases, for each of the next five years and total thereafter are as follows:

	Operating Leases	Lease Payments to be Received from Sublease	Net Operating Lease Payments
	(in thousands)		
2022	$ 7,328	$ 1,824	$ 5,504
2023	6,955	307	6,648
2024	8,167	—	8,167
2025	8,293	—	8,293
2026	6,571	—	6,571
Thereafter	12,200	—	12,200
Total	$ 49,514	$ 2,131	$ 47,383

In arriving at the operating lease liabilities, the Company applied incremental borrowing rates ranging from 6.65% to 7.25%, which were based on the remaining lease term at either the date of adoption of ASC 842 or the effective date of any subsequent lease term extensions. As of December 31, 2021, the remaining lease terms ranged from 4.70 years to 9.59 years. As of December 31, 2021, the following represents the difference between the remaining undiscounted minimum rental commitments under non-cancelable leases and the operating lease liabilities:

	Operating Leases (in thousands) Total
Undiscounted minimum rental commitments	$ 49,514
Present value adjustment using incremental borrowing rate	(10,673)
Operating lease liabilities	$ 38,841

Manufacturing Agreements

As a result of the Merger, the Company's contractual obligations include Keryx's commercial supply agreements with BioVectra Inc., or BioVectra, and Siegfried Evionnaz SA, or Siegfried, to supply commercial drug substance for Auryxia.

Pursuant to the Manufacture and Supply Agreement with BioVectra and the Product Manufacture and Supply and Facility Construction Agreement with BioVectra, the Company agreed to purchase minimum quantities of Auryxia drug substance annually at predetermined prices. On September 4, 2020, the Company and BioVectra entered into an Amended and Restated Product Manufacture and Supply and Facility Construction Agreement, which provided for reduced minimum quantity commitments and revised the predetermined prices. The price per kilogram decreases with an increase in quantity above the predetermined purchase quantity tiers. In addition, the Manufacture and Supply Agreement with BioVectra and the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement with BioVectra require the Company to reimburse BioVectra for certain costs in connection with construction of a new facility for the manufacture and supply of Auryxia drug substance. These construction costs are recorded in other assets and amortized into drug substance as inventory is released to the Company from BioVectra. The term of the Manufacture and Supply Agreement with BioVectra expires on December 31, 2022. The term of the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement expires on December 31, 2026, after which it automatically renews for successive one-year terms unless either party gives notice of its intention to terminate within a specified time prior to the end of the then-current term. In addition, the

Company and BioVectra each have the ability to terminate these agreements upon the occurrence of certain conditions. As of December 31, 2021, the Company is required to reimburse BioVectra for certain costs in connection with the construction of the new facility and to purchase minimum quantities of Auryxia drug substance annually for a total cost of approximately $83.6 million through the end of the contract term.

Pursuant to the Siegfried Master Manufacturing Services and Supply Agreement, as amended (the most recent amendment having been executed on February 11, 2021), or the Siegfried Agreement, the Company has agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The price per kilogram will decrease with an increase in quantity above the minimum purchase quantity. The term of the Siegfried Agreement expires on December 31, 2022, subject to the Company's option to extend through December 31, 2023 by providing 12 months' prior written notice to Siegfried. The Siegfried Agreement provides the Company and Siegfried with certain termination rights. As of the date of the filing of this Annual Report on Form 10-K, the Company has notified Siegfried that the Company has elected not to exercise the option to extend the term of the Siegfried Agreement through December 31, 2023. As of December 31, 2021, the Company is required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately $15.6 million through the year ending December 31, 2022.

As part of purchase accounting, the Company identified executory contracts in the commercial supply agreements between Keryx and its contract manufacturers for Auryxia, which include future firm purchase commitments. These executory contracts were deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast. The Company regularly reviews its estimate of the excess purchase commitment liability including review of assumptions of expected future demand, estimates of anticipated expiry of inventory under firm purchase commitments that are estimated to expire before they could be sold as well as any modifications to supply agreements during each reporting period. The excess purchase commitment liability relating to these executory contracts was $76.7 million and $55.8 million as of December 31, 2021 and 2020, respectively. During the quarter ended December 31, 2021, the Company completed its annual budget process for 2022, which included the impact of recent activity in regards to the impact of COVID-19 on the Company's growth rates. As a result of this budget process, the Company performed an update of its long-term plan. This update to the Company's long-term plan and related estimates of expiry resulted in a $18.0 million charge to cost of goods sold during the quarter ended December 31, 2021. During the quarter ended December 31, 2021, the Company reduced the excess purchase commitment liability by $12.5 million for inventory received that had been previously identified as excess. During the quarter ended September 30, 2021, the Company recorded a $6.0 million reduction to the excess purchase commitments liability within cost of goods sold primarily due to the settlement of all patent litigation proceedings related to Abbreviated New Drug Applications filed with respect to Auryxia, which allows for generic versions of Auryxia beginning in March 2025. The Company recognized this non-cash gain in accordance with ASC 270 *Interim Reporting*, specifically ASC 270-10-45-6(c) *Other Presentation Matters*, which allows for recovery of losses on the same inventory in later interim periods of the same fiscal year as long as the as long as the recovery of losses does not exceed the previously recognized loss. During the quarter ended June 30, 2021, the Company completed a routine update of its long-range plan and related estimates of expiry. This routine update included the impact of recent activity with regards to the Company's long-term payor contract strategy which continues to focus on contract economics and net revenue growth and resulted in a $30.3 million charge to cost of goods sold during the quarter ended June 30, 2021.The Company considered whether the respective increases in the excess purchase commitment liability were potential indicators of impairment of the Auryxia asset group as of December 31, 2021 and June 30, 2021. As part of its assessments, the Company reviewed the Auryxia net sales and estimated future cash flows included in its long-range plan and concluded that the respective increases in excess purchase commitment liability were not indicators of impairment of the Auryxia asset group as of December 31, 2021 or June 30, 2021. During the first quarter ended March 31, 2021, the Company recorded a non-cash gain to cost of goods sold of $8.9 million driven largely by a reduction in purchase commitments due to the amendment to the Siegfried Agreement.

On April 9, 2019, the Company entered into a Supply Agreement with Esteve Química, S.A., or Esteve, or the Esteve Agreement. The Esteve Agreement includes the terms and conditions under which Esteve will manufacture vadadustat drug substance for commercial use. Pursuant to the Esteve Agreement, the Company provides rolling forecasts to Esteve on a quarterly basis, or the Esteve Forecast. The Esteve Forecast reflects the Company’s needs for vadadustat drug substance produced by Esteve over a certain number of months, represented as a quantity of vadadustat drug substance per calendar quarter. The parties have agreed to a volume-based pricing structure under the Esteve Agreement. The Esteve Agreement has an initial term of four years, beginning April 9, 2019 and ending April 9, 2023. Pursuant to the Esteve Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug substance from Esteve. As of December 31, 2021, the Company has committed to purchase $28.9 million of vadadustat drug substance from Esteve through the fourth quarter of 2022.

On March 11, 2020, the Company entered into a Supply Agreement with Patheon Inc., or Patheon, or the Patheon Agreement. The Patheon Agreement includes the terms and conditions under which Patheon will manufacture vadadustat drug product for

commercial use. Pursuant to the Patheon Agreement, the Company provides Patheon a long-term forecast on an annual basis, as well as short-term forecasts on a quarterly basis, or the Patheon Forecast. The Patheon Forecast reflects the Company's needs for commercial supply of vadadustat drug product produced by Patheon, represented as a quantity of drug product per calendar quarter. The parties have agreed to a volume-based pricing structure under the Patheon Agreement. The Patheon Agreement has an initial term beginning March 11, 2020 and ending June 30, 2023. Pursuant to the Patheon Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug product from Patheon. As of December 31, 2021, the Company had a minimum commitment with Patheon for $4.0 million through the fourth quarter of 2022.

On April 2, 2020, the Company entered into a Supply Agreement with STA Pharmaceutical Hong Kong Limited, a subsidiary of WuXi AppTec, or WuXi STA, or the WuXi STA DS Agreement. The WuXi STA DS Agreement includes the terms and conditions under which WuXi STA will manufacture vadadustat drug substance for commercial use. Pursuant to the WuXi STA DS Agreement, the Company provides rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DS Forecast. The WuXi STA DS Forecast reflects the Company's needs for vadadustat drug substance produced by WuXi STA over a certain number of quarters. The parties have agreed to a volume-based pricing structure under the WuXi STA DS Agreement. The WuXi STA DS Agreement has an initial term of four years, beginning April 2, 2020 and ending April 2, 2024. Pursuant to the WuXi STA DS Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug substance from WuXi STA. As of December 31, 2021, the Company has committed to purchase $29.2 million of vadadustat drug substance from WuXi STA through the third quarter of 2022.

On February 10, 2021, the Company entered into a Supply Agreement with WuXi STA, or the WuXi STA DP Agreement. The WuXi STA DP Agreement includes the terms and conditions under which WuXi STA will manufacture and supply vadadustat drug product for commercial purposes. Pursuant to the WuXi STA DP Agreement, the Company will provide rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DP Forecast. Each WuXi STA DP Forecast will reflect the quantities of vadadustat drug product that the Company expects to order from WuXi STA over a certain number of months, represented as a quantity of vadadustat drug product per calendar quarter. Pursuant to the WuXi STA DP Agreement, the Company has agreed to purchase a certain percentage of global demand for vadadustat drug product from WuXi STA. The parties have agreed to a volume-based pricing structure under the WuXi STA DP Agreement. The vadadustat drug product price will remain fixed for the first 12 months and thereafter shall be annually reviewed by the Company and WuXi STA. The Company will also reimburse WuXi STA for certain reasonable expenses. The WuXi STA DP Agreement has an initial term of four years, beginning February 10, 2021 and ending February 10, 2025. The WuXi STA DP Agreement may be renewed or extended by mutual agreement of the Company and WuXi STA with at least 18 months' prior written notice. The WuXi STA DP Agreement allows the Company to terminate the relationship on 180 calendar days' prior written notice to WuXi STA for any reason. In addition, each party has the ability to terminate the WuXi STA DP Agreement upon the occurrence of certain conditions.

Other Third Party Contracts

Under the Company's agreement with IQVIA to provide contract research organization services for the PRO_2TECT and $INNO_2VATE$ programs, the total remaining contract costs as of December 31, 2021 were approximately $5.0 million, of which Otsuka reimburses a significant portion back to the Company. Substantive performance for the committed work with IQVIA was completed in 2020 and close out activities will be performed throughout 2022. The Company also contracts with various other organizations to conduct research and development activities with remaining contract costs to the Company of approximately $237.8 million at December 31, 2021. The scope of the services under these research and development contracts can be modified and the contracts cancelled by the Company upon written notice. In some instances, the contracts may be cancelled by the third party upon written notice.

Litigation and Related Matters

From time to time, the Company may become subject to legal proceedings and claims which arise in the ordinary course of its business. Consistent with ASC 450, *Contingencies*, the Company's policy is to record a liability if a loss in a significant legal dispute is considered probable and an amount can be reasonably estimated. The Company provides disclosure when a loss in excess of any reserve is reasonably possible, and if estimable, the Company discloses the potential loss or range of possible loss. Significant judgment is required to assess the likelihood of various potential outcomes and the quantification of loss in those scenarios. The Company's estimates change as litigation progresses and new information comes to light. Changes in Company estimates could have a material impact on the Company's results and financial position. As of December 31, 2021, the Company does not have any significant legal disputes that require a loss liability to be recorded. The Company continually monitors the need for a loss liability for litigation and related matters.

17. Net Loss per Share

The shares in the table below were excluded from the calculation of diluted net loss per share, prior to the use of the treasury stock method, due to their anti-dilutive effect:

	Year ended December 31,		
	2021	2020	2019
Warrants	509,611	509,611	509,611
Outstanding stock options	11,398,215	9,386,517	7,670,899
Unvested restricted stock units	4,667,003	4,722,311	4,524,132
Total	16,574,829	14,618,439	12,704,642

18. Subsequent Events

Second Amended and Restated License Agreement with Vifor Pharma

On February 18, 2022, the Company and Vifor Pharma entered into a Second Amended and Restated License Agreement, or the Vifor Second Amended Agreement, which amends and restates the Vifor First Amended Agreement. Pursuant to the
Vifor Second Amended Agreement, the Company granted Vifor Pharma an exclusive license to sell vadadustat to the Supply Group in the United States, or the Territory. Vadadustat is the Company's investigational oral HIF prolyl hydroxylase inhibitor for the treatment of anemia due to CKD, for which the Company has filed a new drug application with the FDA.

Like the Vifor First Amended Agreement, the Vifor Second Amended Agreement is structured as a profit share arrangement between the Company and Vifor Pharma in which the Company will receive approximately 66% of the profit, net of certain pre-specified costs. Under the Vifor Second Amended Agreement, Vifor Pharma will make an upfront payment to the Company of $25 million in lieu of the previously disclosed milestone payment of $25 million that Vifor Pharma was to pay to the Company following approval of vadadustat by the FDA. In addition, Vifor Pharma made an equity investment in the Company as further described below under “Investment Agreement.” The Company currently retains rights to commercialize vadadustat for use in the non-dialysis dependent CKD market and to sell to dialysis organizations outside of the Supply Group. As under the Vifor First Amended Agreement, during the term of the Vifor Second Amended Agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the Territory to the Supply Group.

As under the Vifor First Amended Agreement, the Vifor Second Amended Agreement provides that the Company and Vifor Pharma will enter into a commercial supply agreement for vadadustat pursuant to which the Company will supply all of Vifor Pharma’s requirements for vadadustat in the Territory. Under the Vifor Second Amended Agreement, Vifor Pharma will contribute $40 million to the Working Capital Fund, established to partially fund the Company's costs of purchasing vadadustat from its contract manufacturers, which amount of funding will fluctuate, and which funding the Company will repay to Vifor Pharma over time.

Unless earlier terminated, the Vifor Second Amended Agreement will expire upon the later of the expiration of all patents that claim or cover vadadustat or the expiration of marketing or regulatory exclusivity for vadadustat in the Territory. Vifor Pharma may terminate the Vifor Second Amended Agreement in its entirety upon 30 months’ prior written notice after the first anniversary of the receipt of regulatory approval, if approved, from the FDA for vadadustat for dialysis-dependent CKD patients. The Company may terminate the Vifor Second Amended Agreement in its entirety for convenience, following the earlier of a certain period of time elapsing or following certain specified regulatory events, and upon six months’ prior written notice. If the Company so terminates for convenience, subject to a specified exception, the Company will pay a termination fee to Vifor Pharma. In addition, either party may, subject to a cure period, terminate the Vifor Second Amended Agreement in the event of the other party’s uncured material breach or bankruptcy. The Company may also terminate the Vifor Second Amended Agreement upon the occurrence of certain other events. The Vifor Second Amended Agreement also continues to include a standstill provision and customary representations and warranties.

Investment Agreement

In connection with entering into the Vifor Second Amended Agreement, on February 18, 2022, the Company and Vifor Pharma entered into an investment agreement, or the Second Investment Agreement, pursuant to which Akebia sold an aggregate of 4,000,000 shares of its common stock, par value $0.00001 per share, or the Shares, to Vifor Pharma for a total of $20 million on February 22, 2022.

Vifor Pharma has agreed to a lock-up restriction to not sell or otherwise dispose of the Shares for a period of time following the effective date of the Investment Agreement as well as a customary standstill agreement. In addition, the Second Investment Agreement contains voting agreements made by Vifor Pharma with respect to the Shares. The Shares have not been registered

pursuant to the Act and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Act and/or Rule 506 promulgated thereunder, as the transaction does not involve any public offering within the meaning of Section 4(a)(2) of the Act.

First Amendment and Waiver to Loan Agreement with Pharmakon

On February 18, 2022, in connection with entering into the Vifor Second Amended Agreement, the Company and Pharmakon entered into the First Amendment and Waiver, or the First Amendment and Waiver, which amends and waives certain provisions of the Loan Agreement.

Pursuant to the First Amendment and Waiver, the Collateral Agent and the Lenders agreed to (1) add the Working Capital Fund to the definition of Permitted Indebtedness under the Loan Agreement, as such term is defined in the Loan Agreement. subject to certain rights of notice and acceleration of the loans under the Loan Agreement granted to the Collateral Agent and Lenders in connection with the Company's repayment of the Working Capital Fund to Vifor Pharma, and (2) provide the Company with a waiver with respect to a financial statement covenant included in the Loan Agreement and added a new covenant providing that our Quarterly Reports on Form 10-Q for the fiscal quarters ending June 30, 2022 and September 30, 2022 must not be subject to any qualification as to going concern.

Amendment to Lease Agreement with CLPF One Marina Park Drive LLC

On February 24, 2022, Keryx and the Company entered into an Assignment and Assumption Agreement, pursuant to which the Company assumed all of the rights and responsibilities of Keryx with respect to the One Marina Park Drive Office Lease, dated April 29, 2015, by and between Keryx and Fallon Cornerstone One MPD LLC, or Fallon, or the Boston Lease, for the entire twelfth floor of the building located at One Marina Park Drive, Boston, Massachusetts, or the Premises.

On February 24, 2022, the Company entered into a First Amendment to Lease, or the First Lease Amendment, with CLPF One Marina Park Drive LLC (successor-in-interest to Fallon), or the Landlord, amending the Boston Lease for the Premises.

Pursuant to the First Lease Amendment, the Company has agreed to extend the term of the Boston Lease, as amended, until July 31, 2031. The monthly lease payment for the Premises pursuant to the First Lease Amendment will be $200,122.00 commencing on August 1, 2023, with an annual rent escalation of approximately 2% commencing on August 1, 2024. The First Lease Amendment also includes a Landlord's allowance for certain leasehold improvements to the Premises in an amount of up to $1,954,680.00, provided that such allowance must be used prior to August 1, 2024.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding required disclosure.

As of December 31, 2021, our management, with the participation of Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our Chief Executive Officer and Chief Financial Officer have concluded based upon the evaluation described below that, as of December 31, 2021, our disclosure controls and procedures were not effective because of a material weakness in our internal control over financial reporting relating to our inventory process which is described in more detail below.

Management's Annual Report on Internal Control over Financial Reporting

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Securities Exchange Act of 1934 as a process designed by, or under the supervision of, the Company's Chief Executive Officer and Chief Financial Officer and effected by the Company's

board of directors, management and other personnel to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America and includes those policies and procedures that:

(1) Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets;

(2) Provide reasonable assurance that transactions are recorded as necessary to permit preparation of consolidated financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the issuer are being made only in accordance with authorizations of management and directors; and

(3) Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the Company's consolidated financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

Management conducted an assessment of the effectiveness of our internal control over financial reporting as of December 31, 2021 based on the criteria set forth in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. Based on the assessment, management has concluded that the material weakness in our internal control over financial reporting relating to our inventory process as reported in our Annual Report on Form 10-K for the year ended December 31, 2020 remains un-remediated as of December 31, 2021 and that, our internal control over financial reporting as of December 31, 2021 was not effective due to the following material weakness: the Company did not design and maintain effective controls over the completeness, accuracy, existence and presentation and disclosure of inventory. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis. Specifically, we did not maintain effective controls related to (i) the review of inventory reconciliations, (ii) the validation of the inventory costing, (iii) the periodic assessment of excess and obsolete inventory related reserves and (iv) verification that the existence of all inventories subject to physical inventory counts were correctly counted as of December 31, 2021.

Although during 2021 we strengthened our controls related to (i) the review of inventory reconciliations, (ii) the validation of the inventory costing and (iii) the periodic assessment of excess and obsolete inventory related reserves, further remediation is needed. The control deficiencies described above resulted in certain accounting errors, including in our internal preliminary consolidated financial statements for the year ended December 31, 2021 that were corrected prior to the issuance of such annual consolidated financial statements. Management has taken actions to remediate the deficiencies in its internal control over financial reporting and implemented additional processes and controls designed to address the underlying causes associated with the material weakness. Management is committed to finalizing the remediation of the material weakness during 2022. Management's internal control remediation efforts include the following:

- We have designed and implemented more robust controls throughout 2021 and will continue to improve the precision of our controls in 2022.
- We provided training to individuals within the supply chain, manufacturing, quality and inventory processes, including review documentation requirements, during 2021, and will continue to do so in 2022 including training of all new employees and written standard operating procedures for all key inventory processes.
- We designed controls to address the completeness and accuracy of any key reports utilized in the execution of internal controls.
- Implementing an inventory count policy and standard operating procedures to ensure consistent communication of the inventory count process and adherence to these policies at facilities managed by third party logistics and contract manufacturing organizations.
- We reported regularly during 2021, and will continue to report regularly in 2022, to the audit committee on the progress and results of control remediation.
- We continued to engage an outside firm to assist with performing sufficient testing in 2021 and executed upon a monitoring protocol to allow the Company to validate the operating effectiveness of certain controls over financial reporting to gain assurance that such controls are present and functioning as designed. We will continue to engage an outside firm in 2022 to assist management with performing sufficient testing throughout the year to validate the operating effectiveness of certain controls over financial reporting.

As management continues to evaluate and work to improve its internal control over financial reporting, management may determine it is necessary to take additional measures to address the material weakness. Until the controls have been operating for a sufficient period of time and management has concluded, through testing, that these controls are operating effectively, the material weakness described above will continue to exist.

Management will monitor the progress of the remediation plan and report regularly to the audit committee on the progress and results of the remediation plan, including the identification, status and resolution of internal control deficiencies.

Changes in Internal Control over Financial Reporting

Except as noted in the preceding paragraphs, there have been no changes in the Company's internal control over financial reporting during the fourth quarter of 2021, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Ernst & Young, LLP, the Company's independent registered public accounting firm, has issued an auditor's report on management's assessment of the effectiveness of the Company's internal control over financial reporting as of December 31, 2021. This report is included below.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Akebia Therapeutics, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Akebia Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, because of the effect of the material weakness described below on the achievement of the objectives of the control criteria, Akebia Therapeutics, Inc. (the "Company") has not maintained effective internal control over financial reporting as of December 31, 2021, based on the COSO criteria.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis. The following material weakness has been identified and included in management's assessment. Management has identified deficiencies in internal controls included within the Company's inventory process. Specifically, the Company did not maintain effective controls related to (i) the review of inventory reconciliations, (ii) the validation of the inventory costing (iii) the periodic assessment of excess and obsolete inventory related reserves and (iv) verification that the existence of all inventories subject to physical inventory counts were correctly counted.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes. This material weakness was considered in determining the nature, timing and extent of audit tests applied in our audit of the 2021 consolidated financial statements, and this report does not affect our report dated March 1, 2022, which expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 1, 2022

Item 9B. Other Information

Amendment to Lease Agreement with CLPF One Marina Park Drive LLC

On February 24, 2022, we entered into an Assignment and Assumption Agreement with Keryx, pursuant to which we assumed all of the rights and responsibilities of Keryx with respect to the One Marina Park Drive Office Lease, dated April 29, 2015, by and between Keryx and Fallon Cornerstone One MPD LLC, or Fallon, or the Boston Lease, for the entire twelfth floor of the building located at One Marina Park Drive, Boston, Massachusetts, or the Premises.

On February 24, 2022,we entered into a First Amendment to Lease, or the First Lease Amendment, with CLPF One Marina Park Drive LLC (successor-in-interest to Fallon), or the Landlord, amending the Boston Lease for the Premises.

Pursuant to the First Lease Amendment, we have agreed to extend the term of the Boston Lease, as amended, until July 31, 2031. The monthly lease payment for the Premises pursuant to the First Lease Amendment will be $200,122.00 commencing on August 1, 2023, with an annual rent escalation of approximately 2% commencing on August 1, 2024. The First Lease Amendment also includes a Landlord's allowance for certain leasehold improvements to the Premises in an amount of up to $1,954,680.00, provided that such allowance must be used prior to August 1, 2024.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Director, Executive Officers and Corporate Governance

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) Documents filed as part of this Annual Report on Form 10-K.
(b) Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

Consolidated Statements of Stockholders' Equity

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

(3) Exhibits

The Exhibits listed below are filed as part of this Annual Report on Form 10-K.

Exhibit Number	Description of Exhibit
2.1**	Agreement and Plan of Merger, dated as of June 28, 2018, by and among Akebia Therapeutics, Inc., Alpha Therapeutics Merger Sub, Inc., and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K (001-36352), filed on June 28, 2018)
2.2	First Amendment to Agreement and Plan of Merger, dated as of October 1, 2018, by and among Akebia Therapeutics, Inc., Alpha Therapeutics Merger Sub, Inc. and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K (001-36352), filed on October 1, 2018)
3.1	Ninth Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (001-36352), filed on March 28, 2014)
3.2	Certificate of Amendment of Ninth Amended and Restated Certificate of Incorporation of Akebia Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (001-36352), filed on June 9, 2020)
3.3	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (001-36352), filed on March 28, 2014)
4.1	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
4.2	Fourth Amended and Restated Investors' Rights Agreement, dated March 5, 2014 (incorporated by reference to Exhibit 4.4 to the Company's Annual Report on Form 10-K (001-36352), filed on March 4, 2015)
4.3#	Amendment No. 1 to Fourth Amended and Restated Investors' Rights Agreement, dated June 28, 2017 (incorporated by reference to Exhibit 4.5 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2018)
4.4#	Investment Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated May 12, 2017 (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 8, 2017)
4.5*#	Investment Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated February 18, 2022
4.6	Common Stock Purchase Warrant between Akebia Therapeutics, Inc. and Janssen Pharmaceutica NV, dated February 9, 2017 (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 9, 2017)
4.7	Description of Registrant's Securities (incorporated by reference to Exhibit 4.6 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.1†	Form of Director and Officer Indemnification Agreement (incorporated by reference to Exhibit 10.1 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2018)
10.2	Office Lease Agreement Between MA-Riverview/245 First Street, L.L.C. and Akebia Therapeutics, Inc., dated December 3, 2013 (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.3	First Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated December 15, 2014 (incorporated by reference to Exhibit 10.3 to the Company's Annual Report on Form 10-K (001-36352), filed on March 4, 2015)
10.4	Second Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated November 23, 2015 (incorporated by reference to Exhibit 10.4 to the Company's Annual Report on Form 10-K (001-36352), filed on March 14, 2016)

Exhibit Number	Description of Exhibit
10.5	Third Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated July 25, 2016 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 9, 2016)
10.6	Fourth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc., dated May 1, 2017 (incorporated by reference to Exhibit 10.6 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2018)
10.7	Fifth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc. dated April 9, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 8, 2018)
10.8	Sixth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc. dated November 30, 2020 (incorporated by reference to Exhibit 10.8 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.9	One Marina Park Drive Office Lease dated April 29, 2015, by and between Keryx Biopharmaceuticals, Inc. and Fallon Cornerstone One MPD LLC (incorporated by reference to Exhibit 10.29 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K (000-30929), filed on March 1, 2017)
10.10*	First Amendment to One Marina Park Drive Office Lease, dated February 24, 2022, by and between Keryx Biopharmaceuticals, Inc. and CLPF One Marina Park Drive LLC (successor-in-interest to Fallon Cornerstone One MPD LLC)
10.11*	Assignment and Assumption Agreement, dated February 24, 2022, by and between Keryx Biopharmaceuticals, Inc. and Akebia Therapeutics, Inc.
10.12	Sublease, dated as of September 9, 2019, by and between Keryx Biopharmaceuticals, Inc. and Foundation Medicine, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 12, 2019)
10.13†	Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.14†	Amendment No. 1 to Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.15†	Executive Employment Agreement with John P. Butler, dated September 16, 2013 (incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.16†	Offer Letter to David Spellman, dated as of June 13, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 10, 2020)
10.17†	Form of Non-Statutory Stock Option Agreement for officers (incorporated by reference to Exhibit 10.24 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.18†	Form of Non-Statutory Stock Option Agreement for Non-Employee Directors (incorporated by reference to Exhibit 10.25 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.19†	Amended and Restated Non-Employee Director Compensation Program, effective January 1, 2018 (incorporated by reference to Exhibit 10.13 to the Company's 10-K (001-36352), filed on March 12, 2018)
10.20†	Amended and Restated Non-Employee Director Compensation Program, effective January 30, 2019 (incorporated by reference to Exhibit 10.31 to the Company's Annual Report on Form 10-K (001-36352),filed on March 26, 2019)

Exhibit Number	Description of Exhibit
10.21†	Non-Employee Director Compensation Program, effective January 26, 2021 (incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.22†	Form of Executive Severance Agreement for officers (incorporated by reference to Exhibit 10.27 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.23†	2014 Incentive Plan (incorporated by reference to exhibit 10.29 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.24†	Amendment No. 1 to the Akebia Therapeutics, Inc. 2014 Incentive Plan (incorporated by reference to Exhibit 4.4 to the Company's Registration Statement on Form S-8 (333-229366), filed on January 25, 2019)
10.25†	2014 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.30 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.26†	Amended and Restated 2014 Employee Stock Purchase Plan (incorporated by reference to Appendix A to the Company's Definitive Proxy Statement on Schedule 14A (001-36352), filed with the Securities and Exchange Commission on April 26, 2019)
10.27†	Cash Incentive Plan, effective February 28, 2014 (incorporated by reference to Exhibit 10.31 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.28*†	Amended and Restated Cash Incentive Plan, effective January 19, 2022
10.29†	Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan (incorporated by reference to Exhibit 10.18 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2018)
10.30†	Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan (incorporated by reference to Exhibit 10.29 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.31†	Form of Officer Inducement Award Non-Statutory Stock Option Agreement (incorporated by reference to Exhibit 4.4 to the Company's Registration Statement on Form S-8 (333-222728), filed on January 26, 2018)
10.32†	Form of Inducement Award Non-Statutory Stock Option Agreement for non-officers (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-8 (333-222728), filed on January 26, 2018)
10.33†	Form of Officer Performance-Based Stock Option Award, under the Company's 2014 Incentive Plan, as amended (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 4, 2021)
10.34†	Form of Officer Performance-Based Stock Restricted Stock Unit Award, under the Company's 2014 Incentive Plan, as amended (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 4, 2021)
10.35†!	Form of Officer Cash Bonus Letter Agreement (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 4, 2021)
10.36†	Keryx Biopharmaceuticals, Inc. 1999 Stock Option Plan (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (001-30929), filed on March 21, 2003)
10.37†	Keryx Biopharmaceuticals, Inc. 2004 Long-Term Incentive Plan (incorporated by reference to Annex C to Keryx Biopharmaceuticals, Inc.'s Definitive Proxy Statement on Schedule 14A (000-30929), filed on April 29, 2004)
10.38†	Amendment to the Keryx Biopharmaceuticals, Inc. 2004 Long-Term Incentive Plan dated April 11, 2006 (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on August 9, 2006)

Exhibit Number	Description of Exhibit
10.39†	Keryx Biopharmaceuticals, Inc. 2007 Incentive Plan, (incorporated by reference to Annex D to Keryx Biopharmaceuticals, Inc.'s Definitive Proxy Statement on Schedule 14A (000-30929), filed on April 30, 2007)
10.40†	Keryx Biopharmaceuticals, Inc. Amended and Restated 2013 Incentive Plan (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Current Report on Form 8-K (000-30929), filed on May 27, 2016)
10.41†	Keryx Biopharmaceuticals, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 99.1 to Keryx Biopharmaceuticals, Inc.'s Registration Statement on Form S-8 (333-226005), filed on June 29, 2018)
10.42†	Form of Indemnification Agreement between Keryx Biopharmaceuticals, Inc. and its directors and officers (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on November 9, 2016)
10.43†	Form of Employee Agreement (Confidentiality, Non-Competition, Non-Solicitation and Development Agreement) applicable to officers (incorporated by reference to Exhibit 10.56 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.44†	Keryx Biopharmaceuticals, Inc. Fourth Amended and Restated Directors Equity Compensation Plan (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Current Report on Form 8-K (000-30929), filed on May 27, 2016)
10.45†	Keryx Biopharmaceuticals, Inc. Third Amended and Restated Directors Equity Compensation Plan (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on August 7, 2014)
10.46†	Keryx Biopharmaceuticals, Inc. Director Non-Statutory Stock Option Award Terms and Conditions under the Third Amended and Restated Directors Equity Compensation Plan (incorporated by reference to Exhibit 10.59 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.47†	Master Consulting Services Agreement by and between the Company and Jason A. Amello, dated August 7, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 5, 2020)
10.48#	Master Services Agreement, between Akebia Therapeutics, Inc., and Quintiles, Inc., dated as of June 8, 2015 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 11, 2015)
10.49*!	Collaboration Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated December 11, 2015
10.50#	Letter Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated September 26, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 8, 2017)
10.51#	Collaboration and License Agreement, between Akebia Therapeutics, Inc. and Otsuka Pharmaceutical Co. Ltd., dated December 18, 2016 (incorporated by reference to Exhibit 10.26 to the Company's Annual Report on Form 10-K (001-36352) and filed on March 6, 2017)
10.52#	Collaboration and License Agreement between Akebia Therapeutics, Inc. and Otsuka Pharmaceutical Co. Ltd., dated April 25, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 8, 2017)
10.53#	Research and License Agreement between Akebia Therapeutics, Inc. and Janssen Pharmaceutica NV, dated February 9, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 9, 2017)
10.54*!	Second Amended and Restated License Agreement, dated February 18, 2022, by and between Akebia Therapeutics, Inc. and Vifor (International) Ltd.

Exhibit Number	Description of Exhibit
10.55	Amended and Restated Controlled Equity Offering℠ Sales Agreement, dated November 12, 2019, by and between Akebia Therapeutics, Inc. and Cantor Fitzgerald & Co. (incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K (001-36352), filed on November 12, 2019)
10.56!	Second Amended and Restated License Agreement dated April 17, 2019, by and between Akebia Therapeutics, Inc. and Panion & BF Biotech, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 8, 2019)
10.57#	Amended and Restated Sub-License Agreement, dated June 8, 2009, as amended by the First Amendment thereto, dated June 12, 2013, by and between Keryx Biopharmaceuticals, Inc., Japan Tobacco, Inc. and Torii Pharmaceutical Co., Ltd (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on November 7, 2017)
10.58*!	Master Manufacturing Services Agreement by and between Keryx Biopharmaceuticals, Inc. and Patheon Manufacturing Services LLC and certain of its affiliates, dated September 27, 2016, and related Product Agreement dated September 27, 2016, and related Product Agreement dated October 12, 2016
10.59#	Product Agreement, dated August 29, 2017, by and between Keryx Biopharmaceuticals, Inc. and Patheon Inc. (an affiliate of Patheon Manufacturing Services LLC) related to the Master Manufacturing Services Agreement by and between Keryx Biopharmaceuticals, Inc. and Patheon Manufacturing Services LLC and certain of its affiliates dated November 12, 2016 (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on November 7, 2017)
10.60#	Master Manufacturing Services and Supply Agreement, dated December 20, 2017, by and between Keryx Biopharmaceuticals, Inc. and Siegfried Evionnaz SA (incorporated by reference to Exhibit 10.13 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K (000-30929), filed on February 21, 2018)
10.61	Amendment No. 1 to Master Manufacturing Services and Supply Agreement, dated as of December 21, 2020, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 10.58 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.62	Amendment No. 2 to Master Manufacturing Services and Supply Agreement, dated as of January 29, 2021, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 10.58 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.63!	Amendment No. 3 to Master Manufacturing Services and Supply Agreement, dated as of February 11, 2021, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 10.59 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.64*	Amendment No. 4 to Master Manufacturing Services and Supply Agreement, dated as of December 17, 2021, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc.
10.65#	Exclusive Distribution Agreement between Keryx Biopharmaceuticals, Inc. and Cardinal Health 105, Inc., dated October 16, 2014 and First Amendment to Exclusive Distribution Agreement between Keryx Biopharmaceuticals, Inc. and Cardinal Health 105, Inc., dated April 14, 2015 (incorporated by reference to Exhibit 10.60 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.66#	Manufacture and Supply Agreement between Keryx Biopharmaceuticals, Inc. and BioVectra Inc., dated May 26, 2017 and Amendment to Manufacture and Supply Agreement between Keryx Biopharmaceuticals, Inc. and BioVectra Inc., dated December 11, 2017 (incorporated by reference to Exhibit 10.61 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.67!	Supply Agreement, dated as of April 9, 2019, by and between Akebia Therapeutics, Inc. and Esteve Química, S.A. (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 8, 2019)
10.68!	Loan Agreement, dated November 11, 2019, by and among the Company, Keryx Biopharmaceuticals, Inc., Biopharma Credit plc and Biopharma Credit Investments V (Master) LP (incorporated by reference to Exhibit 10.62 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2020)

Exhibit Number	Description of Exhibit
10.69!*	First Amendment and Waiver, dated February 18, 2022, by and among the Company, Biopharma Credit plc, BCPR Limited Partnership and Biopharma Credit Investments V (Master) LP
10.70!	Guaranty and Security Agreement, dated November 25, 2019, by and between the Company, Keryx Biopharmaceuticals, Inc. and Biopharma Credit plc (incorporated by reference to Exhibit 10.63 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2020)
10.71!	Supply Agreement, dated as of March 11, 2020, by and between Akebia Therapeutics, Inc. and Patheon, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 5, 2020)
10.72!	Supply Agreement, dated as of April 2, 2020, by and between Akebia Therapeutics, Inc. and STA Pharmaceutical Hong Kong Limited (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 10, 2020)
10.73!	Amendment #1 to the Supply Agreement, dated as of April 15, 2021, by and between Akebia Therapeutics, Inc, and STA Pharmaceutical Hong Kong Limited (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 5, 2021)
10.74!	Amended and Restated Product Manufacture and Supply and Facility Construction Agreement between BioVectra, Inc. and Keryx Biopharmaceuticals, Inc., dated September 4, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (001-36352), filed on September 11, 2020)
10.75!	Supply Agreement, dated February 10, 2021, by and between the Company and STA Pharmaceutical Hong Kong Limited (incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 10, 2021)
10.76!	Royalty Interest Acquisition Agreement, dated February 25, 2021, by and between the Company and HealthCare Royalty Partners IV, L.P. (incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 10, 2021)
21.1	List of Subsidiaries (incorporated by reference to Exhibit 21.1 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
23.1*	Consent of Ernst & Young LLP
31.1*	Certification of Principal Executive Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended
31.2*	Certification of Principal Financial Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. 1350
101.INS*	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document)
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Labels Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document

Exhibit Number	Description of Exhibit
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* Filed, or submitted electronically, herewith
† Indicates management contract or compensatory plan
# Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment
! Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K
** The schedules to the Agreement and Plan of Merger have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The Company will furnish copies of such schedules to the Securities and Exchange Commission upon request by the Commission

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

AKEBIA THERAPEUTICS, INC.

Date: March 1, 2022	By:	/s/ John P. Butler
		John P. Butler
		President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report was signed by the following persons on behalf of the registrant and in the capacities and on the date indicated.

Date: March 1, 2022	By:	/s/ John P. Butler John P. Butler *Director, President and Chief Executive Officer (Principal Executive Officer)*
Date: March 1, 2022	By:	/s/ David A. Spellman David A. Spellman *Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer)*
Date: March 1, 2022	By:	/s/ Violetta Cotreau Violetta Cotreau *Senior Vice President, Chief Accounting Officer (Principal Accounting Officer)*
Date: March 1, 2022	By:	/s/ Adrian Adams Adrian Adams *Chairperson and Director*
Date: March 1, 2022	By:	/s/ Ron Frieson Ron Frieson *Director*
Date: March 1, 2022	By:	/s/ Steven C. Gilman Steven C. Gilman *Director*
Date: March 1, 2022	By:	/s/ Michael T. Heffernan Michael T. Heffernan *Director*
Date: March 1, 2022	By:	/s/ Michael Rogers Michael Rogers *Director*
Date: March 1, 2022	By:	/s/ Cynthia Smith Cynthia Smith *Director*
Date: March 1, 2022	By:	/s/ Myles Wolf Myles Wolf *Director*
Date: March 1, 2022	By:	/s/ LeAnne M. Zumwalt LeAnne M. Zumwalt *Director*

Exhibit 4.5

Execution Version

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

INVESTMENT AGREEMENT

By and Between

VIFOR (INTERNATIONAL) LTD. AND
AKEBIA THERAPEUTICS, INC.

Dated as of February 18, 2022

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INVESTMENT AGREEMENT

THIS INVESTMENT AGREEMENT (this "**Agreement**") is dated as of February 18, 2022, by and between Vifor (International) Ltd. (together with its permitted successors and assigns, the "**Investor**"), a corporation established in accordance with Swiss laws and registered in the commercial registry under CH-107.360.718, with its premises at Rechenstrasse 37, 9014 St. Gallen, Switzerland, and Akebia Therapeutics, Inc. (together with its permitted successors and assigns, the "**Company**"), a Delaware corporation, with its principal place of business at 245 First Street, Cambridge, Massachusetts 02142.

WHEREAS, pursuant to the terms and subject to the conditions set forth in this Agreement, the Company desires to issue and sell to the Investor, and the Investor desires to subscribe for and purchase from the Company, certain shares of common stock, par value $0.00001 per share, of the Company (the "**Common Stock**"); and

WHEREAS, in partial consideration for the Investor's willingness to enter into this Agreement, the Company and Investor are entering into the License Agreement;

NOW, THEREFORE, in consideration of the following mutual promises and obligations, and for good and valuable consideration, the adequacy and sufficiency of which are hereby acknowledged, the Investor and the Company agree as follows:

ARTICLE I
Definitions.

1.1. Defined Terms. Capitalized terms used herein but not defined shall have the respective meanings ascribed to them in the License Agreement. When used in this Agreement, the following terms shall have the respective meanings specified therefor below:

"**Affiliate"** shall mean, with respect to any Person, another Person that controls, is controlled by, controlling or is under common control with such Person, with "control" meaning direct or indirect Beneficial Ownership of at least 50% of the voting stock of, or at least a 50% interest in the income of, the applicable entity. Notwithstanding the foregoing, "Affiliates" will not include with respect to the Investor, FMC, FMCNA or any member of the Licensee Supply Group.

"**Agreement"** shall have the meaning set forth in the Preamble, including all Exhibits attached hereto.

"**Beneficial Ownership**" shall mean, with respect to any security, the ownership of such security by any "beneficial owner," as such term is defined in Rule 13d-3 and Rule 13d-5 under the Exchange Act, except that, in calculating the beneficial ownership of any particular "person" (as that term is used in Section 13(d)(3) of the Exchange Act), such "person" will be deemed to have beneficial ownership of all securities that such "person" has the right to acquire by conversion or exercise of other securities (including derivative securities, whether such securities are settled in cash or stock), whether such right is currently exercisable or is exercisable only after

the passage of time. The terms "Beneficially Own," "Beneficially Owned" and "Beneficial Owner" shall have correlative meaning.

"**Business Day"** shall mean any day (other than a Saturday or Sunday) on which the banks in both Cambridge, Massachusetts and Zurich, Switzerland are open for business.

"**Company SEC Documents**" shall mean, for the year in which the Closing occurs
(i) the most recently filed Annual Report on Form 10-K, (ii) any Current Reports on Form 8-K filed by the Company with the SEC since the first day of the then-current fiscal year, (iii) the Quarterly Reports on Form 10-Q filed by the Company with the SEC since the filing date of the Form 10-K referred to above, (iv) the Company's most recently filed definitive proxy statement for the annual meeting of stockholders, and (v) all other statements, reports, schedules, forms and other documents filed by the Company with the SEC since the last day of the prior fiscal year, and all amendments thereto.

"**DOJ"** shall mean the U.S. Department of Justice. "**FTC"** shall mean the U.S. Federal Trade Commission.

"**Governmental Authority"** shall mean any court, agency, department, authority or other instrumentality of any national, state, county, city or other political subdivision.

"**Law"** or "**Laws"** shall mean any applicable law (including common law), statute, rule, regulation, order, judgment or ordinance of any Governmental Authority, including those concerning environmental, health, regulatory and safety matters.

"**License Agreement"** shall mean the Second Amended and Restated License Agreement, of even date herewith, between the Investor and the Company.

"**Lock-Up Period**" shall mean the period beginning on the date of this Agreement and extending until the earliest of (i) [**] and (ii) [**].

"**Material Adverse Effect**" means any change, event or occurrence that has had or is reasonably likely to have (i) a material adverse effect on the business, condition (financial or other), assets, liabilities or results of operations of the Company and its subsidiaries, taken as a whole, or (ii) a material adverse effect on the Company's ability to timely perform its obligations under, or timely consummate the Transaction, *except* to the extent that any such change, event or occurrence results from or arises out of changes occurring in general legal, regulatory, political, economic or business conditions or changes in GAAP or interpretations thereof occurring after such date that, in each case, generally affect the biotechnology or biopharmaceutical industries and have not had or would not be reasonably likely to have a disproportionate effect on the Company and its subsidiaries compared to other participants in the biotechnology or biopharmaceutical industries.

"**Nasdaq"** shall mean The Nasdaq Global Market LLC.

"**Organizational Documents"** shall mean (i) the Ninth Amended and Restated Certificate of Incorporation of the Company, as amended through the date of this Agreement and

(ii) the Amended and Restated Bylaws of the Company, as amended through the date of this Agreement.

"**Person"** shall mean any individual, partnership, limited liability company, firm, corporation, trust, joint venture, unincorporated organization, Governmental Authority or other entity, as well as any "group" within the meaning of Rule 13d-5 of the Exchange Act.

"**Price Per Share**" shall equal $5.00.

"**Public Offering**" shall mean a public offering and sale of Common Stock pursuant to an effective registration statement under the Securities Act.

"**Sale Transaction**" shall mean a transaction between the Company and a Third Party (i) involving the direct or indirect acquisition by such Third Party of [**]% or more of the Company's outstanding shares of Common Stock or consolidated assets (including assets held by subsidiaries), *excluding* a transaction in which (a) [**] or (b) [**], or (ii) involving the sale of substantially all of the Company's rights with respect to *vadadustat*.

"**SEC**" shall mean the United States Securities and Exchange Commission. "**Securities Act**" shall mean the Securities Act of 1933, as amended.

"**Third Party"** shall mean any Person, other than a Governmental Authority, the Investor, the Company or any Affiliate of the Investor or the Company.

"**Transaction"** shall mean the issuance and sale of the Shares by the Company, and the purchase of the Shares by the Investor at the Closing.

1.2. Additional Defined Terms. In addition to the terms defined in Section 1.1, the following terms shall have the respective meanings assigned thereto in the sections indicated below:

Defined Term	**Section**
Common Stock	Recitals
Company	Preamble
Exchange Act	Section 4.7(a)
Closing	Section 2.1
Closing Date	Section 3.1
GAAP	Section 4.7(b)
Investor	Preamble
Irrevocable Proxy	Section 6.2(b)(ii)
Modified Clause	Section 7.8
Rule 144	Section 5.9
Shares	Section 2.1

ARTICLE II
Purchase and Sale of Securities

2.1. Purchase and Sale of Securities. Subject to the terms and conditions of this Agreement, at the closing (the "**Closing**") the Company shall issue and sell to the Investor, free and clear of all liens, other than any liens arising as a result of any action by the Investor, and the Investor shall purchase from the Company, 4,000,000 shares of Common Stock (the "**Shares**") at the Price Per Share, representing an aggregate purchase price of U.S. $20,000,000 (the "**Purchase Price**").

ARTICLE III
Closing; Deliveries.

3.1. Closing. The Closing shall take place by electronic exchange of documents upon execution by all parties of this Agreement (the date of such Closing, the "**Closing Date**").

3.2. Deliveries by the Company. At the Closing, immediately following the execution of this Agreement and delivery of the Purchase Price by the Investor to Company in accordance with Section 3.3, the Company shall deliver to the Investor the Shares, registered in the name of the Investor, by instructing its transfer agent to register such issuance in book-entry form at the time of issuance and by causing its transfer agent to deliver a statement evidencing such issuance as soon as practicable following the Closing. The Company shall also deliver at the Closing: (i) a certificate of the Secretary of the Company dated as of the Closing Date certifying (A) that attached thereto is a true and complete copy of the Amended and Restated Bylaws of the Company as in effect at the time of the actions by the Board of Directors of the Company referred to in clause (B) below, and on the Closing Date; (B) that attached thereto is a true and complete copy of all resolutions adopted by the Board of Directors of the Company authorizing the execution, delivery and performance of this Agreement and the Transaction and that all such resolutions are in full force and effect and are all the resolutions adopted in connection with the transactions contemplated hereby as of the Closing Date; (C) that attached thereto is a true and complete copy of the Company's Ninth Amended Restated Certificate of Incorporation, as amended, as in effect at the time of the actions by the Board of Directors of the Company referred to in clause (B) above, and on the Closing Date; and (D) as to the incumbency and specimen signature of any officer of the Company executing this Agreement on behalf of the Company, (ii) an opinion of counsel to the Company substantially in the form attached hereto as Exhibit A and (iii) a certificate of the Chief Executive Officer of the Company substantially in the form attached hereto as Exhibit B.

3.3. Deliveries by the Investor. At the Closing, the Investor shall deliver, or cause to be delivered, to the Company the Purchase Price by wire transfer of immediately available United States funds to an account designated by the Company. The Company shall notify the Investor in writing of the wiring instructions for such account not less than [**] before the Closing Date.

ARTICLE IV
Representations and Warranties of the Company.

The Company hereby represents and warrants to the Investor as of the date of this Agreement that:

4.1. Organization, Corporate Power and Authority. The Company is a corporation duly incorporated, validly existing and in good standing under the laws of the jurisdiction of its incorporation, with the requisite power and authority to own and use its properties and assets and to carry on its business as currently conducted. The Company has all requisite corporate power and corporate authority to own, lease and operate its properties and assets, to carry on its business as described in the Company SEC Documents and as contemplated to be conducted by this Agreement. The Company has and will have all requisite power and corporate authority to enter into this Agreement and to perform its obligations under and to carry out the Transaction.

4.2. Authorization.

(a) All requisite corporate action required by applicable Law for the authorization, execution and delivery by the Company of this Agreement, and the performance of all obligations of the Company hereunder and thereunder, including the authorization, issuance and delivery of the Closing Shares, has been taken.

(b) This Agreement has been duly executed and delivered by the Company and, upon the due execution and delivery thereof by the Investor, will constitute the valid and legally binding obligation of the Company, enforceable against the Company in accordance with its terms (except as such enforceability may be limited by (i) applicable bankruptcy, insolvency, reorganization, moratorium or other Laws of general application relating to or affecting enforcement of creditors' rights and (ii) rules of Law governing specific performance, injunctive relief or other equitable remedies and limitations of public policy).

4.3. No Conflicts. The execution, delivery and performance of this Agreement, and compliance with the provisions hereof by the Company do not and shall not: (a) violate any provision of applicable Law or any ruling, writ, injunction, order, permit, judgment or decree of any Governmental Authority, (b) constitute a breach of, or default under (or an event which, with notice or lapse of time or both, would become a default under) or conflict with, or give rise to any right of termination, cancellation or acceleration of, any agreement, arrangement or instrument, whether written or oral, by which the Company is bound or (c) violate or conflict with any of the provisions of the Company's Organizational Documents, except in each case as would not have a Material Adverse Effect.

4.4. No Governmental Authority or Third Party Consents. No consent, approval, authorization or other order of or filing with any Governmental Authority is required to be obtained by the Company in connection with the authorization, execution and delivery of this Agreement or with the issuance and sale of the Shares at the Closing, except the filing of a Current Report on Form 8-K and a Notice of Sale of Securities on Form D with the Securities and Exchange Commission to the extent required by applicable Law.

4.5. Capitalization. The authorized capitalization of the Company consists of 350,000,000 shares of Common Stock, of which 174,551,989 shares were issued and outstanding as of September 30, 2021, and 25,000,000 shares of preferred stock, $0.00001 par value, of which no shares are issued and outstanding. The sale and issuance of the Shares will not obligate the Company to issue shares of Common Stock or other securities to any other person and will not result in a right of any holder of securities issued by the Company to adjust the exercise,

conversion, or exchange price or ratio under any such securities. Other than as set forth in the Company SEC Documents, the Company is not a party to any stockholders, voting or similar agreement with any other person.

4.6. Valid Issuance of Shares. When issued and delivered in accordance with the terms hereof against payment therefor, the Shares shall be validly issued, fully paid and nonassessable, free from any liens, encumbrances or restrictions on transfer, including preemptive rights, rights of first refusal or other similar rights, other than as arising pursuant to this Agreement, as a result of any action by the Investor or under federal or state securities Laws. Assuming the accuracy of the representations and warranties of the Investor in this Agreement, the Shares will be issued in compliance with all applicable federal and state securities Laws.

4.7. Company SEC Documents; Financial Statements.

(a) During the one year preceding the date of this Agreement, the Company has filed all required reports, schedules, forms, statements and other documents (including exhibits and all other information incorporated therein), and any required amendments to any of the foregoing, with the SEC. As of their respective filing dates (or date of amendment, if amended), each of the Company SEC Documents (i) complied as to form in all material respects with the requirements of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**") (as the case may be), and the rules and regulations of the SEC promulgated thereunder applicable to such Company SEC Documents, and (ii) contained no untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading.

(b) When filed, the financial statements of the Company included in its most recently filed Annual Report on Form 10-K and in its most recently filed quarterly report on Form 10-Q, complied as to form in all material respects with the published rules and regulations of the SEC applicable with respect thereto, were prepared in accordance with United States generally accepted accounting principles ("**GAAP**") applied on a consistent basis during the periods involved (except as may be indicated in the notes thereto or, in the case of unaudited financial statements, as permitted by Form 10-Q, Form 8-K or any successor form under the Exchange Act, and except that the unaudited financial statements may not contain footnotes and are subject to normal and recurring year-end adjustments that will not, individually or in the aggregate, be material in amount) and fairly present in all material respects the financial position of the Company and its consolidated subsidiaries as of the dates thereof and the results of its operations and cash flows for the periods then ended.

(c) From January 1, 2021 to the date hereof, (i) there have been no events, occurrences or developments that have had or would reasonably be expected to have, either individually or in the aggregate, a Material Adverse Effect and (ii) the Company has not incurred any liabilities other than (A) trade payables, accrued expenses and other liabilities incurred in the ordinary course of business consistent with past practice, (B) liabilities not required to be reflected in the Company's financial statements pursuant to GAAP or disclosed in filings made with the Commission, (C) liabilities to the Investor or its Affiliates and (D) liabilities that would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect.

4.8. Litigation. There is no action, suit, proceeding or investigation pending, or to the knowledge of the Company, threatened which (i) would reasonably be expected to materially adversely affect or successfully challenge the legality, validity or enforceability of this Agreement or (ii) except as specifically disclosed in the Company SEC Documents, would, if there were an unfavorable decision, individually or in the aggregate, have or reasonably be expected to result in a Material Adverse Effect. Except as disclosed in the Company SEC Documents, neither the Company nor, to the knowledge of the Company, any director or officer thereof is or has been since January 1, 2020 the subject of any action, suit, proceeding or investigation involving a claim of violation of or liability under federal or state securities laws or a claim of breach of fiduciary duty relating to actions taken at the Company.

4.9. Investment Company. The Company is not, and is not an Affiliate of, and immediately after receipt of payment for the Shares, will not be or be an Affiliate of, an "investment company" within the meaning of the Investment Company Act of 1940, as amended.

4.10. No General Solicitation. Neither the Company nor any Person acting on behalf of the Company has offered or sold any of the Shares by any form of general solicitation or general advertising (within the meaning of Regulation D of the Securities Act). The Company has offered the Shares for sale only to the Investor.

ARTICLE V
Representations and Warranties of the Investor.

The Investor hereby represents and warrants to the Company as of the date of this Agreement that:

5.1. Organization; Good Standing. The Investor is a company duly organized, validly existing and in good standing under the laws of its jurisdiction of formation. The Investor has and will have all requisite power and authority to enter into this Agreement and to perform its obligations under and to carry out the Transaction.

5.2. Authorization. All requisite action required by applicable Law for the authorization, execution and delivery by the Investor of this Agreement, and the performance of all of its obligations hereunder, including the subscription for and purchase of the Shares, has been taken. This Agreement has been duly executed and delivered by the Investor and, upon the due execution and delivery thereof by the Company, will constitute a valid and legally binding obligation of the Investor, enforceable against the Investor in accordance with its terms (except as such enforceability may be limited by (a) applicable bankruptcy, insolvency, reorganization, moratorium or other Laws of general application relating to or affecting enforcement of creditors' rights and (b) rules of Law governing specific performance, injunctive relief or other equitable remedies and limitations of public policy).

5.3. No Conflicts. The execution, delivery and performance of this Agreement and compliance with the provisions thereof by the Investor do not and shall not: (a) violate any provision of applicable Law or any ruling, writ, injunction, order, permit, judgment or decree of any Governmental Authority, (b) constitute a breach of, or default under (or an event which, with notice or lapse of time or both, would become a default under) or conflict with, or give rise to any

right of termination, cancellation or acceleration of, any agreement, arrangement or instrument, whether written or oral, by which the Investor is bound, or (c) violate or conflict with any of the provisions of the Investor's organizational documents (including any articles or memoranda of organization or association, charter, bylaws or similar documents), except as would not have a material adverse effect on the Investor's ability to perform its obligations or consummate the Transaction in accordance with the terms of this Agreement.

5.4. No Governmental Authority or Third Party Consents. No consent, approval, authorization or other order of any Governmental Authority or other Third Party is required to be obtained by the Investor in connection with the authorization, execution and delivery this Agreement or with the subscription for and purchase of the Shares.

5.5. Purchase Entirely for Own Account. The Shares shall be acquired for investment for the Investor's own account, not as a nominee or agent, and not with a view to the resale or distribution of any part thereof, and the Investor has no, and will have no, intention of selling, granting any participation or otherwise distributing the Shares. The Investor does not have and will not have as of the Closing any contract, undertaking, agreement or arrangement with any Person to sell, transfer or grant participation to a Person any of the Shares.

5.6. Disclosure of Information. The Investor has received all the information from the Company and its management that the Investor considers necessary or appropriate for deciding whether to purchase the Shares hereunder. The Investor further represents that it has had an opportunity to ask questions and receive answers from the Company regarding the Company, its financial condition, results of operations and prospects and the terms and conditions of the offering of the Shares sufficient to enable it to evaluate its investment.

5.7. Investment Experience and Accredited Investor Status. The Investor is an "accredited investor" (as defined in Regulation D under the Securities Act). The Investor has such knowledge and experience in financial or business matters that it is capable of evaluating the merits and risks of the investment in the Shares to be purchased hereunder.

5.8. Acquiring Person. The Investor and its Affiliates collectively Beneficially Own 3,571,429 shares of the Common Stock, which amount does not include any securities that may be owned by employee benefit plans of the Investor or any of its Affiliates.

5.9. Restricted Securities. The Investor understands that the Shares, when issued, shall be "restricted securities" under the federal securities Laws inasmuch as they are being acquired from the Company in a transaction not involving a Public Offering and that under such Laws the Shares may be resold without registration under the Securities Act only in certain limited circumstances. The Investor represents that it is familiar with Rule 144 of the Securities Act ("**Rule 144**"), as presently in effect.

5.10. Legends. The Investor understands that any certificates representing the Shares shall bear the following legends:

(a) "THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933. THEY MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED

OR HYPOTHECATED IN THE ABSENCE OF A REGISTRATION STATEMENT IN EFFECT WITH RESPECT TO THE SECURITIES UNDER THE SECURITIES ACT OR AN OPINION OF COUNSEL (WHICH COUNSEL SHALL BE REASONABLY SATISFACTORY TO THE COMPANY) THAT SUCH REGISTRATION IS NOT REQUIRED OR UNLESS SOLD PURSUANT TO RULE 144 OF THE SECURITIES ACT."; and

(b) "THE SECURITIES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO AND SHALL BE TRANSFERABLE ONLY UPON THE TERMS AND CONDITIONS OF AN INVESTMENT AGREEMENT DATED AS OF FEBRUARY 18, 2022, BY AND BETWEEN AKEBIA THERAPEUTICS, INC. AND VIFOR (INTERNATIONAL) LTD., A COPY OF WHICH IS ON FILE WITH THE SECRETARY OF AKEBIA THERAPEUTICS, INC."

ARTICLE VI
Additional Covenants and Agreements.

6.1. Lock-Up.

(a) During the Lock-Up Period, except in the case of a transfer to an Affiliate that agrees to bound by the same restrictions as the Investor described in this ARTICLE VI, the Investor shall not (i) transfer, offer, pledge, sell, contract to sell, or otherwise dispose of, directly or indirectly any option or contract to purchase, purchase any option or contract to sell, or otherwise dispose of, directly or indirectly any of the Shares, or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the Shares, whether any such transaction is to be settled by delivery of securities, cash or otherwise. For the avoidance of doubt, the restrictions described in clauses (i) and (ii) shall not apply to any shares of Common Stock or any securities convertible into, exercisable for, or exchangeable for shares of Common Stock Beneficially Owned by the Investor or its Affiliates immediately prior to the Closing.

(b) Following the expiration of the Lock-Up Period, the Investor may transfer any Shares only as follows: (i) in a Public Offering, (ii) in accordance with Rule 144 (including the volume limitations contained in clause (e) thereof, regardless of whether such limitations would then be applicable to any such transfer), (iii) pursuant to a tender offer initiated by the Company,
(iv) in a privately negotiated transaction (other than [**]) so long as the transferee agrees to be bound by the same restrictions as the Investor described in this ARTICLE VI or (v) in any transaction between the Company and a Third Party (including a third party tender offer or other business combination transaction) which has been approved by the Company's Board of Directors.

6.2. Additional Agreements of Investor.

(a) Standstill. Except in connection with the acquisition of Shares by the Investor pursuant to the terms of this Agreement, the Investor shall not, without the written consent of the Company, acquire directly or indirectly, in a public or private transaction, including by purchase in the open market, any Common Stock if the Investor's Beneficial Ownership of the Common Stock would thereafter exceed [**] percent ([**]%). In addition, unless approved in advance in writing by the Company, the Investor agrees that it will not, directly or indirectly:

(i) Make any statement or proposal to the Company (other than a non-public statement or proposal delivered directly to the Chief Executive Officer or Chairman of the Board of Directors) or to any of the Company's stockholders regarding, or make any public announcement, proposal or offer (including an "solicitation" of "proxies" as such terms are defined or used in Regulation 14A of the Exchange Act) with respect to, or otherwise solicit, seek or offer to effect (including, for the avoidance of doubt, indirectly by means of communication with the press or media) (A) any business combination, merger, tender offer, exchange offer or similar transaction in the Company, (B) any restructuring, recapitalization, liquidation or similar transaction involving the Company, (C) any acquisition of any of the Company's equity securities or assets or rights or options to acquire equity securities or assets, (D) any proposal to seek representation on the Board of Directors of the Company or otherwise seek to control or influence the management, Board of Directors or policies of the Company or (E) any proposal, arrangement or other statement that is inconsistent with this Section 6.2;

(ii) Instigate, encourage or assist any Third Party (including forming a "group" with any such third party) to do, or enter into any discussions or agreements with any Third Party with respect to, any of the actions set forth in clause (i) above; or

(iii) Take any action which would reasonably be expected to require the Company or any of is Affiliates to make a public announcement regarding any of the actions set forth in clause (i) above.

Notwithstanding the foregoing provisions, the restrictions set forth in this Section 6.2(a) shall terminate and be of no further force and effect (x) if [**], provided that the provisions of this Section 6.2(a) shall be revived if [**]; (y) upon [**]; or (z) so long as the Investor's Beneficial Ownership remains less than [**] percent ([**]%) of the Company's Common Stock, provided that the provisions of this Section 6.2(a) shall be revived at any time when the Investor's Beneficial Ownership equals [**] percent ([**]%) or more of the Company's Common Stock.

(b) Voting Agreements.

(i) Until the later of (x) [**], Investor shall either (A) vote (or cause to be voted) all of the shares of Common Stock it Beneficially Owns at meetings of the Company's stockholders, (1) as recommended by the Company in its definitive proxy statement or (2) in the same proportion as votes cast by the stockholders of the Company with respect to the applicable matter (such proportion determined without inclusion of the votes cast by Investor) on any matter presented for approval by the Company's stockholders or (B) [**]. Any such vote shall be cast by Investor in accordance with such procedures relating thereto so as to ensure that it is duly counted, including for purposes of determining that a quorum is present and for purposes of recording the results of such vote.

(ii) Until the expiration of the period described in the foregoing clause (i), Investor appoints [**] of the Company, or their respective designees, and each of them individually, its proxy and attorneys-in-fact, with full power of substitution and resubstitution (the "**Irrevocable Proxy**") to vote the shares of Common Stock as recommended by the Company in its definitive proxy statement. Investor shall take such further action or execute such other instruments as may be necessary to effectuate the intent of this proxy. This proxy and power of

attorney shall be irrevocable during the term of this Agreement, and shall revoke any and all prior proxies granted by Investor with respect to the Shares. The proxy and power of attorney granted hereunder shall terminate upon the termination of the voting agreements in Section 6.2(b)(i).

Notwithstanding the foregoing, the Irrevocable Proxy shall be effective if, at any annual or special meeting of stockholders of the Company and at any adjournments or postponements of any such meeting, the Investor (A) fails to appear or otherwise fails to cause the Shares to be counted as present for purposes for calculating a quorum, or (B) fails to vote such Shares in accordance with this Section 6.2, in each case, at least [**] prior to the date of such stockholders' meeting.

(c) Information Black Outs. From time to time, material non-public information (including information the Company has designated as material and non-public) regarding the Company may be available to Investor but not publicly disclosed. While in possession of such material non-public information and until, (i) the second trading day following the date on which the material non-public information has been publicly disclosed or (ii) the Company notifies the Investor that the information is no longer material (which it shall do promptly after it has made such determination), Investor shall not effect any sales of Common Stock on Nasdaq, regardless of whether the standstill provisions of Section 6.2(a) are then currently in effect or the Lock-Up Period has then expired.

6.3. Form D; Blue Sky Filings. If an offering hereunder qualifies under Regulation D, the Company agrees to timely file a Form D with respect to the Shares as required under Regulation D and to provide a copy thereof, promptly upon request of the Investor. If an offering hereunder does not qualify under Regulation D, the Company shall take such action as the Company shall reasonably determine is necessary in order to obtain an exemption for, or to qualify the Shares for, sale to the Investor at the Closing under applicable securities or "Blue Sky" laws of the states of the United States, and shall provide evidence of such actions promptly upon request of the Investor.

6.4. Public Disclosure. The parties hereto agree that the provisions of Section 14.3 of the License Agreement shall be applicable to the parties to this Agreement with respect to any public disclosures regarding the Transaction or regarding the parties hereto or their Affiliates (it being understood that the provisions of Section 14.3 of the License Agreement shall be read to apply to disclosures of information relating to this Agreement and the Transaction).

6.5. Rule 144. The Company shall use its reasonable best efforts to file the reports required to be filed by it under the Securities Act and the Exchange Act and the rules and regulations adopted by the SEC thereunder in a timely manner in accordance with the requirements of the Securities Act and the Exchange Act (and, if at any time the Company is not required to file such reports, the Company will, upon the request of the Investor, make available such information necessary to permit sales pursuant to Rule 144).

ARTICLE VII
Miscellaneous.

7.1. Governing Law; Submission to Jurisdiction. This Agreement shall be governed by and construed in accordance with the Laws of the State of Delaware, without regard to the conflict of laws principles thereof that would require the application of the Law of any other jurisdiction.

Any action brought, arising out of, or relating to this Agreement shall be brought in the Court of Chancery of the State of Delaware. Each party hereby irrevocably submits to the exclusive jurisdiction of said Court in respect of any claim relating to the validity, interpretation and enforcement of this Agreement, and hereby waives, and agrees not to assert, as a defense in any action, suit or proceeding in which any such claim is made that it is not subject thereto or that such action, suit or proceeding may not be brought or is not maintainable in such courts, or that the venue thereof may not be appropriate or that this Agreement may not be enforced in or by such courts. The parties hereby consent to and grant the Court of Chancery of the State of Delaware jurisdiction over such parties and over the subject matter of any such claim and agree that mailing of process or other papers in connection with any such action, suit or proceeding in the manner provided in Section 7.3 or in such other manner as may be permitted by Law, shall be valid and sufficient thereof.

7.2. Waiver. Waiver by a party of a breach hereunder by the other party shall not be construed as a waiver of any subsequent breach of the same or any other provision. No delay or omission by a party in exercising or availing itself of any right, power or privilege hereunder shall preclude the later exercise of any such right, power or privilege by such party. No waiver shall be effective unless made in writing with specific reference to the relevant provision(s) of this Agreement and signed by a duly authorized representative of the party granting the waiver.

7.3. Notices. All notices, instructions and other communications hereunder or in connection herewith shall be in writing, shall be sent to the address of the relevant party set forth below and shall be (a) delivered personally, (b) sent by registered or certified mail, return receipt requested, postage prepaid, (c) sent via a reputable nationwide overnight courier service or (d) sent by facsimile transmission or electronic mail, with a confirmation copy to be sent by registered or certified mail, return receipt requested, postage prepaid. Any such notice, instruction or communication shall be deemed to have been delivered upon receipt if delivered by hand, three (3) Business Days after it is sent by registered or certified mail, return receipt requested, postage prepaid, one (1) Business Day after it is sent via a reputable nationwide overnight courier service or when transmitted with electronic confirmation of receipt, if transmitted by facsimile or electronic mail (if such transmission is made during regular business hours of the recipient on a Business Day; or otherwise, on the next Business Day following such transmission). Either party may change its address by giving notice to the other party in the manner provided above.

If to the Investor:

Vifor Pharma
Flughofstrasse 61, 8152 Glattbrugg, Switzerland Facsimile: [**]
Attention: [**]

With a copy to: [**] E-Mail: [**]

If to the Company:

Akebia Therapeutics, Inc.

245 First Street
Cambridge, MA 02142 Facsimile: [**] Attention: [**]

with a copy to:

Ropes & Gray LLP Prudential Tower 800 Boylston Street
Boston, MA 02199 Attention: [**]
E-Mail: [**]

7.4. Specific Performance. The parties hereto agree that irreparable damage would occur if any provision of this Agreement were not performed in accordance with the specific terms hereof or were otherwise breached. It is accordingly agreed that the parties shall be entitled, without posting a bond or similar indemnity, to an injunction or injunctions to prevent breaches of this Agreement or to enforce specifically the performance of the terms and provisions hereof, in addition to any other remedy to which it is entitled at law or in equity. Each of the Company and the Investor agrees that it will not oppose the granting of an injunction, specific performance and other equitable relief when expressly available pursuant to the terms of this Agreement on the basis that the other party has an adequate remedy at law or an award of specific performance is not an appropriate remedy for any reason at law or equity.

7.5. Entire Agreement. This Agreement contains the entire agreement among the parties with respect to the subject matter hereof and thereof and supersedes all prior and contemporaneous arrangements or understandings, whether written or oral, with respect hereto and thereto.

7.6. Amendments. No provision in this Agreement shall be supplemented, deleted or amended except in a writing executed by an authorized representative of each of the Investor and the Company.

7.7. Headings; Nouns and Pronouns; Section References. Headings in this Agreement are for convenience of reference only and shall not be considered in construing this Agreement. Whenever the context may require, any pronouns used herein shall include the corresponding masculine, feminine or neuter forms, and the singular form of names and pronouns shall include the plural and vice-versa. References in this Agreement to a section or subsection shall be deemed to refer to a section or subsection of this Agreement unless otherwise expressly stated.

7.8. Severability. If, under applicable Laws, any provision hereof is invalid or unenforceable, or otherwise directly or indirectly affects the validity of any other material provision(s) of this Agreement in any jurisdiction ("**Modified Clause**"), then this Agreement shall endure and that the Modified Clause shall be enforced in such jurisdiction to the maximum extent permitted under applicable Laws in such jurisdiction; provided that the parties shall consult and use all reasonable efforts to agree upon, and hereby consent to, any valid and enforceable

modification of this Agreement as may be necessary to avoid any unjust enrichment of either party and to match the intent of this Agreement as closely as possible, including the economic benefits and rights contemplated herein.

7.9. Assignment. Except for an assignment of this Agreement or any rights hereunder by the Investor to an Affiliate or by the Company to a successor or direct or indirect parent company in connection with a transaction that does not give rise to a termination of this Agreement, neither this Agreement nor any of the rights or obligations hereunder may be assigned by either the Investor or the Company without (a) the prior written consent of Company in the case of any assignment by the Investor or (b) the prior written consent of the Investor in the case of an assignment by the Company.

7.10. Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns.

7.11. Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original but which together shall constitute one and the same instrument.

7.12. Third Party Beneficiaries. None of the provisions of this Agreement shall be for the benefit of or enforceable by any Third Party, including any creditor of any party hereto. No Third Party shall obtain any right under any provision of this Agreement or shall by reason of any such provision make any claim in respect of any debt, liability or obligation (or otherwise) against any party hereto.

7.13. No Strict Construction. This Agreement has been prepared jointly and will not be construed against either party.

7.14. Survival of Warranties. The representations and warranties of the Company and the Investor contained in this Agreement shall survive the Closing and expire on the [**] of the effective date of this Agreement.

7.15. Remedies. The rights, powers and remedies of the parties under this Agreement are cumulative and not exclusive of any other right, power or remedy which such parties may have under any other agreement or Law. No single or partial assertion or exercise of any right, power or remedy of a party hereunder shall preclude any other or further assertion or exercise thereof.

7.16. Expenses. Each party shall pay its own fees and expenses in connection with the preparation, negotiation, execution and delivery of this Agreement and the Transaction.

7.17. Term. If not earlier terminated by mutual written consent of the Company and the Investor, the obligations set forth in this Agreement shall expire at such times as set forth herein.

(Signature Page Follows)

IN WITNESS WHEREOF, the parties have executed and delivered this Agreement as of the date first above written.

VIFOR (INTERNATIONAL) LTD.

By: /s/ Abbas Hussain Name: Abbas Hussain
Title: Chief Executive Officer

By:/s/ Christoph Springer Name: Dr. Christoph Springer

/s/ Dr. Oliver P. Kronenberg
Approved by Legal: Dr. Oliver P. Kronenberg 18-Feb-22

Title: Chief Strategy Officer

AKEBIA THERAPEUTICS, INC.

By:/s/ John P. Butler Name: John P. Butler
Title: President and Chief Executive Officer

Exhibit 10.10

FIRST AMENDMENT TO LEASE

THIS FIRST AMENDMENT TO LEASE (this "**First Amendment**") is made as of February 24, 2022 (the "**Effective Date**"), by and between **CLPF ONE MARINA PARK DRIVE LLC** (successor-in-interest to Fallon Cornerstone One MPD LLC), a Delaware limited liability company ("**Landlord**"), and **AKEBIA THERAPEUTICS, INC.** (successor-in-interest to Keryx Biopharmaceuticals, Inc.), a Delaware corporation ("**Tenant**") for certain premises located in the building at One Marina Park Drive, Boston, Massachusetts (the "**Building**").

RECITALS

A. Landlord and Tenant are parties to that certain One Marina Park Drive Office Lease dated as of April 29, 2015, as affected by that certain Assignment and Assumption Agreement of even date herewith (the "**Lease**"), for certain premises consisting of approximately 27,323 rentable square feet (the "**Premises**") on the entire twelfth (12th) floor of the Building.

B. Landlord and Tenant wish to enter into this First Amendment to (i) extend the term of the Lease, and (ii) amend certain other terms and conditions of the Lease as hereinafter set forth.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing Recitals, which are incorporated herein by this reference, the mutual promises and conditions contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant hereby agree as follows:

1. Capitalized Terms. All of the foregoing recitals are true and correct. Unless otherwise defined herein, all capitalized terms used in this First Amendment shall have the meanings ascribed to them in the Lease, and all references herein or in the Lease to the "Lease" or "this Lease" or "herein" or "hereunder" or similar terms or to any section thereof shall mean the Lease, or such section thereof, as amended by this First Amendment.

2. Extension of Term. The Term of the Lease, which but for this First Amendment is scheduled to expire on February 28, 2023, is hereby extended for an additional period (the "**Extension Term**") of eight (8) years and five (5) months, commencing on March 1, 2023 (the "**Extension Term Commencement Date**") and expiring on July 31, 2031 (the "**Extension Term Expiration Date**"). The Extension Term shall be upon all of the terms and conditions of the Lease, except as otherwise expressly modified or amended by this First Amendment and except that (i) the Allowance shall not be applicable to (or payable by Landlord) with respect to the Extension Term, and (ii) during the Extension Term, the new rentable square footage of the Premises is amended to be 27,924 rentable square feet. As of the Effective Date, "Term" or "Term of this Lease", as used in the Lease, shall be deemed to refer to the Term of the Lease, as herein extended for the Extension Term.

3. Monthly Base Rent. Commencing on August 1, 2023 (the "**Extension Term Rent Commencement Date**") and thereafter during the Extension Term, Tenant shall pay Monthly Base Rent in accordance with the following schedule:

Time Period	Annual Base Rent Per Square Foot	Annual Base Rent	Monthly Base Rent
August 1, 2023 – July 31, 2024	$86.00	$2,401,464.00	$200,122.00
August 1, 2024 – July 31, 2025	$87.72	$2,449,493.28	$204,124.44
August 1, 2025 – July 31, 2026	$89.47	$2,498,483.15	$208,206.93
August 1, 2026 – July 31, 2027	$91.26	$2,548,452.81	$212,371.07
August 1, 2027 – July 31, 2028	$93.09	$2,599,421.86	$216,618.49
August 1, 2028 – July 31, 2029	$94.95	$2,651,410.30	$220,950.86
August 1, 2029 – July 31, 2030	$96.85	$2,704,438.51	$225,369.88
August 1, 2030 – July 31, 2031	$98.79	$2,758,527.28	$229,877.27

4. Additional Rent; Utilities.

(a) During the Extension Term, Tenant shall continue to pay Additional Rent and other charges, including the Escalation Increase except that effective as of the Extension Term Commencement Date, (i) the "**Base Year**" for the Extension Term shall be amended to the calendar year 2023 for Operating Expenses and fiscal year 2024 for Taxes, and (ii) the Tenant's Pro Rata Share is hereby amended to 5.929% (27,924/470,949).

(b) Tenant shall continue to pay for all utilities serving the Premises which are separately metered and not otherwise provided by Landlord under the Lease, pursuant to Sections 7(D) and 7(E) of the Lease.

5. Condition of Premises; Extension Term Improvements. Tenant is in possession of the Premises and has accepted the Premises in their as-is condition without any obligation on Landlord's part to perform any additions, alterations, improvements, demolition or other work therein or pertaining thereto, or to provide any construction or other allowances as set forth in the Lease. Notwithstanding the foregoing, Landlord hereby agrees to provide Tenant an allowance not to exceed One Million Nine Hundred Fifty-Four Thousand Six Hundred Eighty and 00/100 Dollars ($1,954,680.00) (which is equal to $70.00 per rentable square foot of the Premises) (the

"**Extension Term Allowance**") in connection with the Extension Term Improvements (as hereinafter defined) as more specifically described in the work letter and specifications attached hereto as **Exhibit A** (the "**Work Letter**"). Tenant acknowledges and agrees that Landlord shall have no obligation to pay or fund any unfunded portion of the Extension Term Allowance in the event that the Extension Term Allowance has not been requisitioned by Tenant within eighteen (18) months following the Extension Term Commencement Date (the "**Reimbursement Deadline**"), subject to a day for day extension of such Reimbursement Deadline if Tenant's performance of the Extension Term Improvements is actually delayed due to a construction moratorium imposed after the Extension Term Commencement Date by any governmental authority having jurisdiction over the Building. If Tenant fails to properly requisition the full Extension Term Allowance on or before the Reimbursement Deadline, Tenant shall be deemed to have waived any right to the balance thereof.

6. Option to Extend. Landlord and Tenant hereby agree that Tenant shall continue to have its option to extend the Term for one (1) period of five (5) years as set forth in Exhibit F of the Lease, except that subsection (a)(i) of Exhibit F of the Lease is hereby amended to require that Tenant shall give Tenant's Notice to Extend to exercise the Extension Option no later than twelve (12) months prior to the Extension Term Expiration Date.

7. Security Deposit.

(a) Landlord is currently holding a Security Deposit in the amount of Three Hundred Ninety-Four Thousand Four Hundred Seventy-Five and 82/100 Dollars ($394,475.82) (the "**Existing Letter of Credit**"). Not later than thirty (30) days after Tenant's execution of this First Amendment, Tenant shall deliver to Landlord either (i) an amendment to the Existing Letter of Credit, or (ii) a substitute Letter of Credit, in either case, to increase the face amount of the Letter of Credit required under the Lease to One Million and 00/100 Dollars ($1,000,000.00) (the "**Increased Letter of Credit Amount**"), and which shall comply with and be held subject to and in compliance with all of the requirements of Article 23 of the Lease. Provided and on the condition that no event of default has occurred at any time on or before the applicable review dates set forth below (each an "**Applicable Review Date**"), the amount of the Security Deposit shall be reduced to the amount set forth below corresponding to the Applicable Review Date:

APPLICABLE REVIEW DATE	NEW REDUCED AMOUNT
August 1, 2026	$800,488.00
August 1, 2027	$600,366.00

Within ten (10) business days after Landlord receives a written request from Tenant for reduction of the Letter of Credit pursuant to this Section 7, Landlord shall confirm to Tenant in writing whether the conditions for such reduction have been satisfied as of the Applicable Review Date and, if such conditions have been satisfied and there is no default of Tenant then in existence, Tenant thereafter shall provide Landlord with an amendment to the Existing Letter of Credit or a substitute Letter of Credit, as applicable, meeting all of the requirements of Article 23 of the Lease, to accomplish such authorized reduction of the Letter of Credit, and, in the case of a substitute Letter of Credit, Landlord shall surrender the prior Letter of Credit within five (5) business days of Landlord's receipt of the substitute Letter of Credit in compliance with such requirements. In no event shall any Letter of Credit have automatic reduction provisions.

(b) The third (3rd) paragraph of Section 23(f) of the Lease is hereby deleted in its entirety.

8. Broker Indemnity. Each party represents and warrants to the other party that it has not dealt with any broker in connection with this First Amendment other than CBRE and Jones Lang LaSalle Incorporated (the "**Broker**"), and insofar as such party knows, no other broker(s) negotiated this First Amendment or is entitled to any commission in connection herewith. Each party covenants and agrees to defend, with counsel approved by the other party, indemnify and save the other party harmless from and against any and all cost, expense or liability for any compensation, commission or charges claimed by any broker other than the Broker, or agent or finder who dealt with such party. Landlord shall be responsible for paying any commission due to the Broker in connection with this First Amendment, pursuant to a separate agreement.

9. Ratification. Except as expressly modified by this First Amendment, the Lease shall remain in full force and effect, and as further modified by this First Amendment, is expressly ratified and confirmed by the parties hereto. This First Amendment shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns, subject to the provisions of the Lease regarding assignment and subletting.

10. Governing Law; Interpretation and Partial Invalidity. This First Amendment shall be governed and construed in accordance with the laws of the Commonwealth of Massachusetts. If any term of this First Amendment, or the application thereof to any person or circumstances, shall to any extent be invalid or unenforceable, the remainder of this First Amendment, or the application of such term to persons or circumstances other than those as to which it is invalid or unenforceable, shall not be affected thereby, and each term of this First Amendment shall be valid and enforceable to the fullest extent permitted by law. The titles for the paragraphs are for convenience only and are not to be considered in construing this First Amendment. This First Amendment contains all of the agreements of the parties with respect to the subject matter hereof, and supersedes all prior dealings between them with respect to such subject matter. No delay or omission on the part of either party to this First Amendment in requiring performance by the other party or exercising any right hereunder shall operate as a waiver of any provision hereof or any rights hereunder, and no waiver, omission or delay in requiring performance or exercising any right hereunder on any one occasion shall be construed as a bar to or waiver of such performance or right on any future occasion.

11. Counterparts and Authority. This First Amendment may be executed in multiple counterparts (including by .pdf file exchanged via email or other electronic transmission), each of which shall be deemed an original and all of which together shall constitute one and the same document. Landlord and Tenant each warrant to the other that the person or persons executing this First Amendment on its behalf has or have authority to do so and that such execution has fully obligated and bound such party to all terms and provisions of this First Amendment.

[The remainder of this page is intentionally left blank.]

IN WITNESS WHEREOF, the parties hereto have hereunto set their hands and seals, or caused this First Amendment to be signed by their proper officers the day and year first above written.

LANDLORD:

CLPF ONE MARINA PARK DRIVE LLC,
a Delaware limited liability company

By: CLPF-MA REIT, LLC,
a Delaware limited liability company,
its Sole Member

By: CLPF-Holdings, LLC,
a Delaware limited liability company,
its General Partner

By: Clarion Lion Properties Fund Holdings REIT, LLC,
a Delaware limited liability company,
its Sole Member

By: Clarion Lion Properties Fund, LP,
a Delaware limited partnership,
its Managing Member

By: Clarion Partners LPF GP, LLC,
a Delaware limited liability company,
its General Partner

By: Clarion Partners, LLC,
a New York limited liability company,
its Sole Member

By: /s/ Brian Collins
Name: Brian Collins
Title: Authorized Signatory

TENANT:
AKEBIA THERAPEUTICS, INC., a Delaware corporation

By: /s/ David A. Spellman
Name: David A. Spellman
Title: Senior Vice President, Chief Financial Officer and Treasurer

EXHIBIT A

WORK LETTER

1.

a. Tenant shall, at Tenant's expense, submit to Landlord conceptual or schematic plans ("**Tenant's Preliminary Plans")** depicting Tenant's proposed improvements to the Premises (the "**Extension Term Improvements**"). Landlord shall not unreasonably withhold, delay or condition its approval of Tenant's Preliminary Plans. Within five (5) business days of receipt of Tenant's Preliminary Plans, Landlord shall approve Tenant's Preliminary Plans or designate by written notice to Tenant the specific changes required to be made to Tenant's Preliminary Plans, which Tenant shall make within five (5 business days of receipt. This process shall be repeated until Tenant's Preliminary Plans are finally approved by Landlord.

b. Upon Landlord's approval of Tenant's Preliminary Plans, Tenant shall, at Tenant's expense, submit to Landlord final and complete dimensioned and detailed plans and drawings of partition layouts (including openings), ceiling and lighting layouts, colors, mechanical and electrical circuitry plans and any and all other information as may be reasonably necessary to complete the Extension Term Improvements in accordance with this Exhibit A and that are a logical evolution of the Tenant's Preliminary Plans approved by Landlord (such plans are collectively referred to herein as "**Tenant's Extension Term Plans**"). The partition layout, and ceiling and lighting layout plans shall be l'0" = 1/8" scale. Tenant shall submit Tenant's Extension Term Plans and any other plans required by this Exhibit A to Landlord in form, quality and quantity acceptable for the purposes of filing for a building permit with the Inspectional Services Department of the City of Boston ("**ISD**"), and such plans shall be signed and sealed by an architect licensed in the Commonwealth of Massachusetts.

c. Landlord shall not unreasonably withhold, delay or condition its approval of Tenant's Extension Term Plans. Within ten (10) business days of receipt of Tenant's Extension Term Plans, Landlord shall approve Tenant's Extension Term Plans or designate by written notice to Tenant the specific changes required to be made to Tenant's Extension Term Plans, which Tenant shall make within ten (10) business days of receipt. This procedure shall be repeated until Tenant's Extension Term Plans are finally approved by Landlord, except that the review and revision period for each of Landlord and Tenant, respectively, shall be five (5) business days after the foregoing initial 10-business day period for Landlord's initial review of and Tenant's initial revisions to Tenant's Extension Term Plans.

d. [Intentionally omitted].

e. All plans, drawings and specifications with respect to the Premises required to be submitted by Tenant to Landlord shall comply with and conform to the Building plans filed with the ISD and the Office of Interior Standards 2009 (the receipt of which Tenant hereby acknowledges) and with all the rules, regulations and/or other requirements of any governmental department having jurisdiction over the construction of the Building and/or Premises. Tenant shall prepare drawings in accordance with preexisting conditions and field measurements.

f. Landlord's review of Tenant's Extension Term Plans is solely to protect the interests of Landlord in the Building and the Premises, and Landlord shall be neither the guarantor of, nor responsible for, the correctness or accuracy of Tenant's Extension Term Plans, or the compliance of Tenant's Extension Term Plans with applicable requirements of any

governmental authority. Landlord's review and approval of any submissions shall not be deemed to be an approval of the adequacy for any particular purpose or system capacity or the cost of the Extension Term Improvements.

g. In the event Landlord engages a third party engineer or consultant to review Tenant's Extension Term Plans, Tenant shall reimburse Landlord for all actual, out-of-pocket costs incurred by Landlord in connection with such review pursuant to this Exhibit A, subject to the Extension Term Allowance; provided that no costs reimbursed hereunder shall be duplicative of costs reimbursed under the Lease.

2.

a. Tenant shall, at its expense (except for the Extension Term Allowance), in accordance with the terms and conditions of this Exhibit A, be responsible for the construction of Extension Term Improvements. The term "**Substantial Completion**" shall mean when Tenant has obtained a temporary or final certificate of occupancy from ISD with respect to the Premises as improved in accordance with the terms and conditions of this Exhibit A. After completion of Tenant's Extension Term Plans, Tenant shall submit Tenant's Extension Term Plans to the appropriate governmental body for a building permit. Landlord shall reasonably cooperate with Tenant, at no cost to Landlord, in obtaining such permit, including, without limitation, executing any permit applications required by governmental authorities. Tenant shall deliver a copy of the building permit to Landlord prior to the commencement of construction of the Extension Term Improvements. Tenant shall not make any material changes to Tenant's Extension Term Plans once finally approved by Landlord without Landlord's consent.

b. Tenant shall select a contractor (the "**Contractor**"), subject to the approval of Landlord, which approval will not be unreasonably withheld, conditioned or delayed and shall be granted or denied within ten (10) days of request for such approval. With its request for approval of the Contractor, Tenant shall furnish to Landlord such information concerning the proposed Contractor's background and experience as Landlord may reasonably require. A price for a construction contract based on Tenant's Extension Term Plans shall be mutually agreed upon by Tenant and the Contractor. Tenant shall enter into an agreement with the Contractor to build the Extension Term Improvements, at Tenant's sole cost, except for the Extension Term Allowance. The construction contract will provide for progress payments, no more frequently than once per calendar month, and each progress payment will be funded as follows: Landlord will fund the percentage of each progress payment equal to a fraction expressed as a percentage, the numerator of which is the Extension Term Allowance and the denominator of which is the total cost of the Extension Term Improvements; and Tenant will fund the remainder. Ten percent (10%) of each progress payment shall be retained by Landlord until Tenant delivers, or causes to be delivered, to Landlord a certificate of occupancy or certificate of completion, in form and substance reasonably satisfactory to Landlord, with respect to the Premises together with final and unconditional waivers of mechanic's liens concerning the work for all labor and services performed and all material furnished in connection with the work, signed by the Contractor and all subcontractors, suppliers, and laborers involved in the work. Notwithstanding anything contained herein or in the Lease to the contrary, Landlord shall have no obligation to disburse any portion of the Extension Term Allowance during any period of time that Tenant is in default of its obligations under the Lease (continuing uncured following receipt of notice thereof from Landlord) and the expiration of any applicable cure period. If Landlord declines to fund any progress payment on the basis of a default and Tenant cures such default in accordance with the terms and provisions of the Lease, then, subject to the provisions set forth herein, Landlord shall fund such progress payment that was declined as provided herein.

c. If the cost of the design and construction of the Extension Term Improvements is less than the Extension Term Allowance, the difference shall be retained by

Landlord. In the event that Tenant requests any changes to Tenant's Extension Term Plans, Landlord shall not unreasonably withhold, delay or condition its consent to any such changes, provided the changes do not adversely affect the Building's structure, systems, equipment or appearance.

d. The Extension Term Allowance will be applied to the construction of the Extension Term Improvements, and up to thirty percent (30%) of the Extension Term Allowance may be used (i) for "soft" costs associated with the design of the Extension Term Improvements, including without limitation, any project manager retained by Tenant or, at Tenant's written election, (ii) as a credit against Tenant's Base Rent obligations payable under the Lease following the Extension Term Rent Commencement Date, and for no other purpose. All costs attributable to the Extension Term Improvements in excess of the Extension Term Allowance shall be paid for by Tenant. Tenant may requisition the Extension Term Allowance solely for soft costs reimbursement at any time following the Effective Date of this First Amendment and may requisition the Extension Term Allowance for the hard costs to perform the Extension Term Improvements from and after the Extension Term Commencement Date.

3.

a. Before beginning the Extension Term Improvements, Tenant shall pay for and deliver to Landlord satisfactory evidence of the insurance coverage(s) required to be maintained by Tenant under Article 8 of the Lease. Landlord and the Contractor shall be named as additional insureds in such liability policies or certificates of insurance and the same shall remain in effect during the period of the performance of the Extension Term Improvements.

b. All the Extension Term Improvements shall be in accordance with the Project Documents and applicable rules and regulations of any governmental department or bureau having jurisdiction thereover, and all the Extension Term Improvements shall be completed free of all liens and encumbrances. All permits which may be required by Tenant for the Extension Term Improvements shall be procured and paid for by Tenant and Landlord shall reasonably cooperate with Tenant, at no cost to Landlord, to obtain any such permits. No plans and/or specifications required to be filed by Tenant pursuant to any work contemplated to be performed by it within the Premises shall be filed or submitted to any governmental authority having jurisdiction thereover without first having obtained Landlord's approval of same, which approval shall not be unreasonably withheld, conditioned or delayed.

c. Upon completion of the Extension Term Improvements, Tenant will remove all debris and excess materials in connection with such Extension Term Improvements from the Building and the Premises.

d. Without limiting the applicability of Article 5.E. of the Lease, the labor employed by Tenant or the Contractor shall always be harmonious and compatible with the labor employed by Landlord or any contractors or sub-contractors of Landlord. Should such labor be incompatible with such Landlord's labor as shall be determined by the sole judgment of Landlord, to be exercised in good faith, Landlord may require Tenant to withdraw from the Premises until the completion of the Building and/or Premises by Landlord.

e. In the event Tenant or the Contractor shall enter upon the Premises or any other part of the Building, as may be permitted by Landlord, Tenant shall indemnify and save Landlord free and harmless from and against any and all claims for personal injury or property damage arising from or out of any entry thereon or the performance of the Extension Term Improvements or for any other reason whatsoever arising out of said entry or such work.

f. Extension Term Improvements which Landlord reasonably determines are specialized to Tenant's use and occupancy of the Premises, including, without limitation, wiring and cabling, shall, at the election of Landlord (which election shall be made in writing at the time of Landlord's approval of Tenant's Extension Term Plans hereunder), either (1) be removed by Tenant at its expense before the expiration or earlier termination of the term of the Lease or (2) remain upon the Premises and be surrendered therewith without disturbance, molestation or injury upon the expiration or earlier termination of the Lease. If Landlord requires the removal of all or part of the specialized Extension Term Improvements, Tenant, at its expense, shall repair any damage to the Premises or the Building caused by such removal. If Tenant fails to remove any specialized Extension Term Improvements upon Landlord's request, then Landlord may (but shall not be obligated to) remove the same and the out-of-pocket cost of such removal and repair of any damage caused by the same incurred by Landlord shall be charged to Tenant and paid within thirty (30) days after written demand therefor.

4. Tenant shall be responsible for the maintenance, repair and replacement of all Extension Term Improvements unless the same is necessitated by the negligent acts of Landlord.

5. Tenant shall, as soon as reasonably practicable, notify Landlord of the name of the individual that Tenant authorizes as Tenant's representative to act on its behalf and represent its interests with respect to all matters which pertain to the construction of Extension Term Improvements, and to make decisions binding upon Tenant with respect to such matters. Landlord hereby authorizes Shawn Carroll to be Landlord's representative in connection with construction of the Extension Term Improvements. Tenant hereby expressly recognizes and agrees that no other person claiming to act on behalf of the Landlord is authorized to do so, and any costs, expenses liabilities or obligations incurred or paid by Tenant in reliance on the discretion of any such other person shall be Tenant's sole responsibility.

6. In the event of a conflict between the terms and provisions of the Lease and the terms and provisions of this Exhibit A, the terms and provisions of this Exhibit A shall control.

Exhibit 10.11

ASSIGNMENT AND ASSUMPTION OF LEASE

This Assignment and Assumption of Lease (the "Assignment") is made on February 24, 2022 (the "Effective Date") by and between KERYX BIOPHARMACEUTICALS, INC., a Delaware corporation ("Assignor") and AKEBIA THERAPEUTICS, INC., a Delaware corporation ("Assignee"). Assignee and Assignor may be referred to from time to time in this Agreement individually as a "Party" and collectively as the "Parties".

RECITALS:

This Assignment is made with regard to the following facts:

A. CLPF One Marina Park Drive LLC (successor-in-interest to Fallon Cornerstone One MPD LLC), a Delaware limited liability company ("Landlord"), as landlord, and Assignor, as tenant, are parties to that certain Office Lease dated as of April 29, 2015 (the "Lease"), pursuant to which Landlord has leased to Assignor that certain premises containing approximately 27,323 rentable square feet (the "Premises") comprising the entire twelfth (12th) Floor of One Marina Park Drive, Boston, MA (the "Building"). A copy of the Lease is attached hereto as Exhibit A and incorporated by reference; and

B. Assignor was acquired by Assignee on or about December 12, 2018 whereby Assignor became a wholly owned subsidiary of Assignee. In connection therewith, Assignor desires to assign its rights, title, and interest in, to, and under the Lease and the Premises to Assignee, and Assignee desires to accept that assignment on, and subject to, all of the terms and conditions in this Assignment.

NOW THEREFORE, in consideration of the mutual covenants contained in this Assignment, and for valuable consideration, the receipt and sufficiency of which are acknowledged by the Parties, the Parties agree as follows.

1. Assignment and Assumption. Assignor assigns to Assignee all of its rights, title and interest to, and under the Lease and the Premises (including all of Assignor's rights, title, and interest in and to any prepaid rents that have been paid by Assignor under the Lease for any period before or after the Effective Date and including the parking access devices for the Parking Garage). Assignee accepts this Assignment, assumes all of Assignor's rights and obligations under the Lease pursuant to the terms of the Lease, and agrees to be bound by all of the provisions of the Lease and to perform all of the obligations of the tenant under the Lease as a direct obligation to Landlord from and after the Effective Date of the Assignment.

2. Further Assurances. Each party to this Assignment will, at its own cost and expense, execute and deliver such further documents and instruments and will take such other actions as may be reasonably required or appropriate to evidence or carry out the intent and purposes of this Assignment.

3. Governing Law. This Assignment will be governed by, and construed in accordance with, the laws of the Commonwealth of Massachusetts.

4. Captions. Captions to the sections in this Assignment are included for convenience only and do not modify any of the terms of this Assignment.

5. Severability. If any term or provision of this Assignment is, to any extent, held to be invalid or unenforceable, the remainder of this Assignment will not be affected, and

each term or provision of this Assignment will be valid and be enforced to the fullest extent permitted by law.

6. Capitalized Terms. All terms spelled with initial capital letters in this Assignment that are not expressly defined in this Assignment will have the respective meanings given such terms in the Lease.

7. Execution in Counterparts. This Assignment may be executed in any number of counterparts and transmitted by facsimile to the other Party, each of which when so executed shall be deemed an original and all of which shall constitute together one and the same instrument, and shall be effective upon execution by all of the Parties.

IN WITNESS WHEREOF, Assignor and Assignee have executed this Assignment on the date first written above:

ASSIGNOR:
KERYX BIOPHARMACEUTICALS, INC.

By: /s/ John P. Butler

Name: John P. Butler
Title: Authorized Officer, as President and Chief Executive Officer of Akebia Therapeutics, Inc., parent company of Keryx Biopharmaceuticals, Inc.

ASSIGNEE:
AKEBIA THERAPEUTICS, INC.

By: /s/ David A. Spellman

Name: David A. Spellman
Title: Senior Vice President, Chief Financial Officer and Treasurer

EXHIBIT A
[Lease]

Incorporated by reference to Exhibit 10.9 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2021 as filed with the Securities and Exchange Commission.

AKEBIA THERAPEUTICS, INC.

CASH INCENTIVE PLAN

January 19, 2022

This Cash Incentive Plan (the "Plan") has been established to advance the interests of Akebia Therapeutics, Inc. (the "Company") by providing for the grant of Cash Incentive Awards to eligible employees of the Company and its subsidiaries.

I. ADMINISTRATION

The Plan will be administered by the Committee and its delegates (the Committee and its delegates, to the extent of such delegation, are referred to herein as the "Administrator"). For purposes of the Plan, "Committee" means the Compensation Committee of the Board of Directors of the Company.

The Administrator has the authority to interpret the Plan and Cash Incentive Awards, to determine eligibility for Cash Incentive Awards, to determine the terms of and the conditions applicable to any Cash Incentive Award, and generally to do all things necessary to administer the Plan. Any interpretation or decision by the Administrator with respect to the Plan or any Cash Incentive Award will be final and conclusive as to all parties.

II. ELIGIBILITY; PARTICIPANTS

Executive officers and other employees of the Company and its subsidiaries shall be eligible to participate in the Plan. The Administrator will select, from among those eligible, the persons who will from time to time participate in the Plan (each, a "Participant"). Participation with respect to one Cash Incentive Award under the Plan will not entitle an individual to participate with respect to a subsequent Cash Incentive Award or Cash Incentive Awards, if any.

III. GRANT OF AWARDS

The term "Cash Incentive Award" as used in the Plan means an award opportunity, including an annual cash compensation award, that is granted to a Participant with respect to a specified performance period (consisting of the Company's fiscal year or such other period as the Administrator may determine, each a "Performance Period") payable if certain performance conditions are satisfied. A Participant who is granted a Cash Incentive Award will be entitled to a payment, if any, under the Cash Incentive Award if all conditions to payment have been satisfied in accordance with the Plan and the terms of the Cash Incentive Award. By accepting (or, under such rules as the Administrator may prescribe, being deemed to have accepted) a Cash Incentive Award, the Participant agrees (or will be deemed to agree) to the terms of the Cash Incentive Award and the Plan. For each Cash Incentive Award, the Administrator shall establish the following:

(a) the Performance Criteria (as defined in Section IV below) applicable to the Cash Incentive Award, subject to adjustment as provided herein;

(b) the amount or amounts that will be payable if the Performance Criteria are achieved, subject to adjustment as provided herein; and

(c) such other terms and conditions as the Administrator deems appropriate, subject in each case to the terms of the Plan.

IV. PERFORMANCE CRITERIA

As used in the Plan, "Performance Criteria" means specified criteria, other than the mere continuation of employment or the mere passage of time, the satisfaction of which is a condition for the vesting, payment or full enjoyment of a Cash Incentive Award. A Performance Criterion and any targets with respect thereto determined by the Administrator may be applied to a Participant or Participants on an individual basis, a business unit or division, or the Company as a whole. A Performance Criterion will mean a determinable measure of performance relating to any or any combination of the following (measured either absolutely or by reference to an index or indices and determined either on a consolidated basis or, as the context permits, on a divisional, subsidiary, line of business, project or geographical basis or in combinations thereof): sales; revenues; assets; expenses; earnings before or after deduction for all or any portion of interest, taxes, depreciation, amortization or equity expense, whether or not on a continuing operations or an aggregate or per share basis; return on equity, investment, capital, capital employed or assets; one or more operating ratios; operating income or profit, including on an after-tax basis; net income; borrowing levels, leverage ratios or credit rating; market share; capital expenditures; cash flow; stock price; stockholder return; sales of particular products or services; customer acquisition or retention; acquisitions and divestitures (in whole or in part); joint ventures, strategic alliances, licenses or collaborations; spin-offs, split-ups and the like; reorganizations; recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings; manufacturing or process development; achievement of clinical trial or research objectives, regulatory or other filings or approvals or other product development milestones or any other performance measure selected by the Administrator. The Administrator may establish that one or more of the Performance Criteria applicable to such Cash Incentive Award may or will be adjusted to reflect events (for example, the impact of charges for restructurings, discontinued operations, mergers, acquisitions, extraordinary items, and other unusual or non-recurring items, and the cumulative effects of tax or accounting changes, each as defined by U.S. generally accepted accounting principles or such other factors as the Administrator determines) occurring during the Performance Period that affect the applicable Performance Criteria.

V. CONFIRMATION OF PERFORMANCE; AMOUNT PAYABLE UNDER AWARDS

The Administrator will determine whether and to what extent, if at all, the Performance Criteria applicable to each Cash Incentive Award granted for the Performance Period have been satisfied and apply any adjustments, whether established at the time the Performance Criteria were established or that the Administrator otherwise determines to be appropriate. The Administrator shall then determine the actual payment, if any, under each Cash Incentive Award. The Administrator may, in its reasonable discretion, after determining the amount that would otherwise be payable under any Cash Incentive Award for a Performance Period, increase or reduce (including to zero) the actual payment, if any, to be made under such Cash Incentive Award. The Administrator may exercise the discretion described in the immediately preceding sentence either in individual cases or in ways that affect more than one Participant, as appropriate. In each case, the Administrator's discretionary determination, which may affect different Cash Incentive Awards differently, will be binding on all parties.

VI. PAYMENT UNDER AWARDS

Except as otherwise determined by the Administrator or as otherwise provided in this Section VI, all payments under the Plan will be made, if at all, not later than March 15th of the calendar year following the calendar year in which the Performance Period ends or the end of the calendar year in which the Administrator approves the amount payable to a Participant, if earlier; provided, that the Administrator may authorize elective deferrals of any Cash Incentive Award payments in accordance with the deferral rules of Section 409A of the Code and the regulations thereunder ("Section 409A"). The Administrator may, but need not, provide that a Cash Incentive Award payment will not be made unless the Participant has remained employed with

the Company and its subsidiaries through the date of payment. Cash Incentive Awards under the Plan are intended either to qualify for exemption from, or to comply with the requirements of, Section 409A.

VII. TAX WITHHOLDING; LIMITATION ON LIABILITY

All payments under the Plan will be subject to reduction for applicable tax and other legally or contractually required withholdings.

Neither the Company nor any affiliate, nor the Administrator, nor any person acting on behalf of the Company, any affiliate, or the Administrator, will be liable for any adverse tax or other consequences to any Participant or to the estate or beneficiary of any Participant or to any other holder of a Cash Incentive Award that may arise or otherwise be asserted with respect to a Cash Incentive Award, including, but not limited to, by reason of the application of Section IX below or any acceleration of income or any additional tax (including any interest and penalties) asserted by reason of the failure of a Cash Incentive Award to satisfy the requirements of Section 409A or by reason of Section 4999 of the Code.

VIII. AMENDMENT AND TERMINATION

The Committee may amend the Plan at any time and from time to time. The Committee may at any time terminate the Plan.

IX. MISCELLANEOUS

Cash Incentive Awards held by a Participant are subject to forfeiture, termination and rescission, and a Participant will be obligated to return to the Company payments received with respect to Cash Incentive Awards, in each case (a) to the extent provided by the Administrator in connection with (i) a breach by the Participant of a Cash Incentive Award agreement or the Plan, or any non-competition, non-solicitation, confidentiality or similar covenant or agreement with the Company or any of its affiliates or (ii) an overpayment to the Participant of incentive compensation due to inaccurate financial data, (b) in accordance with any applicable Company clawback or recoupment policy, as such policy may be amended and in effect from time to time, or (c) as otherwise required by law or applicable stock exchange listing standards, including, without limitation, Section 10D of the Securities Exchange Act of 1934, as amended. Each Participant, by accepting a Cash Incentive Award pursuant to the Plan, agrees to return the full amount required under this Section IX at such time and in such manner as the Administrator shall determine in its sole discretion.

No person shall have any claim or right to be granted a Cash Incentive Award, nor shall the selection for participation in the Plan for any Performance Period be construed as giving a Participant the right to be retained in the employ or service of the Company or its affiliates for that Performance Period or for any other period. The loss of a Cash Incentive Award will not constitute an element of damages in the event of termination of employment for any reason, even if the termination is in violation of an obligation of the Company or any affiliate to the Participant.

The Plan shall be effective upon adoption of the Plan by the Board of Directors of the Company (the “Effective Date”) and shall supersede and replace the Company’s current cash incentive plan.

Exhibit 10.49

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Triple asterisks denote omissions.

COLLABORATION AGREEMENT

BY AND BETWEEN

AKEBIA THERAPEUTICS, INC.

AND

MITSUBISHI TANABE PHARMA CORPORATION

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COLLABORATION AGREEMENT

THIS **COLLABORATION AGREEMENT** (this "**Agreement**") is made and entered into as of December 11, 2015 ("**Effective Date**") between Akebia Therapeutics, Inc., a company organized and existing under the laws of the State of Delaware, United States of America with its principal offices at 245 First Street, Suite 1100, Cambridge, MA 02142, U.S.A. ("**Akebia**"), and Mitsubishi Tanabe Pharma Corporation, a company organized and existing under the laws of Japan, with its principal offices at 3-2-10 Dosho-machi, Cho-ku, Osaka, Japan ("**Licensee**").

Akebia and Licensee may be referred to herein individually as a "**Party**" and collectively as the "**Parties**".

RECITALS

WHEREAS, Akebia is the owner of, or otherwise controls, the Akebia Technology and the Licensed Compound and the Licensed Product in the Territory as defined below;

WHEREAS, Licensee has expertise in the development of biopharmaceutical products and has regulatory and commercial capabilities in the Territory, and is interested in obtaining an exclusive license to Develop and Commercialize the Licensed Compound and the Licensed Product in the Territory; and

WHEREAS, the Parties desire to [***] for the Licensed Compound and the Licensed Product and collaborate to Develop and Commercialize the Licensed Compound and the Licensed Product in the Territory, and Akebia wishes to grant Licensee an exclusive license to develop, use, sell, offer to sell and import the Licensed Compound and the Licensed Product in the Territory for this purpose.

NOW THEREFORE, the Parties agree as follows:

ARTICLE I.

DEFINITIONS

Section 1.01 "Affiliate" means, with respect to an entity, any corporation or other business entity controlled by, controlling, or under common control with such entity, with "control" meaning direct or indirect beneficial ownership of at least fifty percent (50%) of the voting stock of, or at least a fifty percent (50%) interest in the income of, the applicable entity. Notwithstanding the foregoing, "Affiliates" shall not include, with respect to an entity, bona fide venture capital investors in such entity or bona fide institutional investors in such entity, which institutional investors routinely make venture capital investments for the potential financial return on such investments and not with any view to acquisition or for any other strategic purpose, or Affiliates of such venture capital or institutional investors.

Section 1.02 "Akebia Inventions" means all Inventions that (a) are made prior to or during the Term by one or more employees of Akebia or any Affiliate of Akebia, or persons contractually required to assign or license patent rights covering such Inventions to Akebia or any Affiliate of Akebia, and (b) are not Joint Inventions.

Section 1.03 "Akebia Know-How" means all Know-How that is both (a) Controlled as of the Effective Date and during the Term by Akebia or any of its Affiliates; and (b) [***]; or (ii) [***]. For the avoidance of doubt, Akebia Know-How shall include any Know-How developed during the Global Phase 3 Program.

Section 1.04 "Akebia Patents" means all Patents (including any Joint Patents) that both (a) are Controlled as of the Effective Date or during the Term by Akebia or any of its Affiliates in the Territory, and (b) cover a Licensed Compound or a Licensed Product or their respective Development, manufacture, use, design, registration, offer for sale, sale or importation. All Akebia Patents as of the Effective Date are listed in Exhibit A.

Section 1.05 "Akebia Reserved Dispute" means any dispute with respect to the [***] including any decision that [***] including, without limitation, decisions regarding any [***] of the Licensed Compound or Licensed Product or the [***] of the Licensed Compound or Licensed Product in the Territory. Notwithstanding the foregoing, once the Joint Steering Committee has determined to [***] any dispute relating to the [***].

Section 1.06 "Akebia Technology" means Akebia Know-How and Akebia Patents.

Section 1.07 "Akebia Trademark" means one or more trademarks selected by Akebia or its licensees under which (i) Akebia or its licensees will market any Licensed Product outside the Territory and/or (ii) Licensee will Commercialize the Licensed Product inside the Territory if the global brand name is used in accordance with Section 6.05 (Trademarks and International Nonproprietary Name) hereof, as well as the trademarks for the Akebia company name and logo, and all trademark registrations and applications therefor, and all goodwill associated therewith.

Section 1.08 "API" means active pharmaceutical ingredient, which is also commonly referred to as drug substance. For the avoidance of doubt, API shall include any prodrug form.

Section 1.09 "Business Day" means a calendar day in which the corporate headquarters of both Akebia and Licensee are open for business.

Section 1.10 "Commercialization" or "Commercialize" means, with respect to a Licensed Product or a Combination Product or Bundled Product, any and all activities directed to the marketing, promotion, distribution, offering for sale, and sale of such Licensed Product, Combination Product, or Bundled Product in the Territory, and interacting with Regulatory Authorities regarding the foregoing.

Section 1.11 "Commercialization Plan" means the annual plan for Commercialization of the Licensed Product, Combination Product and/or Bundled Product in the Territory by Licensee and the activities to be conducted by Licensee relating thereto including, without limitation, detailed plans for sales and marketing after launch.

Section 1.12 "Commercially Reasonable Efforts" means, with respect to the Development and/or Commercialization of a Licensed Compound or Licensed Product, those efforts and resources, including reasonably necessary personnel, equivalent to the efforts that a research-based biopharmaceutical company would typically devote to a product of similar market potential, profit potential and strategic value and at a comparable stage in development or product life to such Licensed Product, based on conditions then prevailing and taking into account issues of safety and efficacy, product profile, difficulty in developing the Licensed Product, competitiveness of alternative Third Party products in the marketplace, the patent or other proprietary position of the Licensed Product, the regulatory structure involved and the potential profitability of the Licensed Product marketed or to be marketed.

Section 1.13 "Confidential Information" means Know-How and any technical, scientific, trade, research, manufacturing, business, financial, marketing, product, supplier, intellectual property and other information that may be disclosed by one Party to the other Party, regardless of whether such information is specifically designated as confidential and regardless of whether such information is in written, oral, electronic, or other form.

Section 1.14 "Controlled" means, with respect to a Party or its Affiliate, and any Know-How, Patent or other intellectual property right, that such Party or Affiliate, as the case may be, owns or has a license to such intellectual property right and has the ability to grant to the other Party a license or sublicense to, or a right of access with respect to, such Know-How, Patent or other intellectual property right without violating the terms of any pre-existing agreement or other pre-existing arrangements with any Third Party.

Section 1.15 "Cost of Goods Sold" or "COGS" means the fully burdened cost of all direct materials and labor and fully allocated manufacturing overhead directly attributable to the manufacture, storage, packaging, and shipping of a Licensed Product, calculated in accordance with U.S. GAAP and Akebia's or its suppliers', as applicable, then-prevailing standard procedure for calculating COGS as reflected in Akebia's or its suppliers', as applicable, audited financial statements. COGS includes, without limitation, all bulk API, work in process (where applicable) and transfer prices paid by Akebia, Licensed Product testing and yield loss costs, quality control, quality assurance, or other testing of Licensed Products, together with all reasonably allocated indirect costs and overhead applicable to manufacturing of Licensed Product, quality control or technical operations functions, less costs of goods returned in accordance with Akebia's, or its suppliers', return policy.

Section 1.16 "DD-CKD Indication" means the treatment of anemia in dialysis patients with chronic kidney disease.

Section 1.17 "Development" means all internal and external research, development and regulatory activities regarding a Licensed Compound and Licensed Product, as the case may be. This includes (a) research, preclinical testing, toxicology, route of synthesis, non-clinical activities, formulation and clinical studies of Licensed Compound and Licensed Product; and (b) preparation, submission, review, and development of data or information for the purpose of submission to a governmental authority to obtain authorization to conduct clinical trials and Regulatory Approval of Licensed Product. Development shall include development and regulatory activities for additional forms, formulations, or indications for a Licensed Product after Regulatory Approval of such Licensed Product, including clinical trials initiated following receipt of Regulatory Approval or any clinical trial to be conducted after a Regulatory Approval which was mandated by the applicable Regulatory Authority as a condition of such Regulatory Approval with respect to an approved indication. "Develop", "Developing" and "Developed" shall be construed accordingly.

Section 1.18 "Development Plan" means the plan setting out activities to be undertaken by Licensee and Akebia, and their Affiliates, licensees and sublicensees, in Developing the Licensed Compound and Licensed Product together with timelines and, in the [***], budgets, for such activities including, without limitation, the proposed clinical trials, regulatory plans, and manufacturing plans as well as outlining the key elements involved in obtaining Regulatory Approval in the Territory.

Section 1.19 "Distributor" means any Third Party appointed by Licensee or its Affiliates to distribute, market, offer for sale and/or sell the Licensed Product in the Territory.

Section 1.20 "Dollars" or "$" means the legal tender of the U.S.

Section 1.21 "FDA" means the U.S. Food and Drug Administration or any successor agency thereto.

Section 1.22 "FD&C Act" means the U.S. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 et seq., as amended from time to time.

Section 1.23 "Field" means the treatment, prevention and/or diagnosis of any diseases or conditions in humans, including, but not limited to, anemia.

Section 1.24 "First Commercial Sale" means, for each Licensed Product in the Territory, the first sale for end use or consumption to a Third Party of such Licensed Product in the Territory by Licensee, its Affiliate or its permitted sublicensee after the granting of Regulatory Approval in the Field for such Licensed Product by the relevant Regulatory Authorities. First Commercial Sale excludes any sale or other distribution for use in a clinical trial or other Development activity, or for compassionate or named-patient use.

Section 1.25 "Global Phase 3 DD-CKD Study" means the Phase 3 global clinical studies for the DD-CKD Indication, known informally as the $INNO_2VATE$ study, consisting of a conversion study and a correction study, and known formally as the "Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat Compared to Epoetin Alfa in the Maintenance Treatment of Anemia of CKD in Subjects with Dialysis-Dependent Chronic Kidney Disease ($INNO_2VATE$ – Conversion)" and the "Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat for the Correction of Anemia in Subjects with Incident Dialysis-Dependent Chronic Kidney Disease ($INNO_2VATE$ – Correction)".

Section 1.26 "Global Phase 3 NDD-CKD Study" means the Phase 3 global clinical studies for the NDD-CKD Indication, known informally as the PRO_2TECT study, consisting of a conversion study and a correction study, and known formally as the "Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat for the Maintenance Treatment of Anemia in Subjects with Non-Dialysis Dependent Chronic Kidney Disease (PRO_2TECT – Conversion)" and the "Phase 3, Randomized, Open-Label, Active-Controlled Study Evaluating the Efficacy and Safety of Oral Vadadustat for the Correction of Anemia in Subjects with Non-Dialysis-Dependent Chronic Kidney Disease (PRO_2TECT – Correction)".

Section 1.27 "Global Phase 3 Program" means the Global Phase 3 NDD-CKD Study and the Global Phase 3 DD-CKD Study collectively, as well as any other studies that (i) generate data required to obtain Regulatory Approval of the Licensed Product both inside and outside of the Territory and that (ii) are approved by the JSC.

Section 1.28 "Good Clinical Practices" or "GCP" means the then-current good clinical practice standards, practices, and procedures promulgated or endorsed by the applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

Section 1.29 "Good Laboratory Practices" or "GLP" means the then-current good laboratory practice standards, practices, and procedures promulgated or endorsed by the applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

Section 1.30 "Good Manufacturing Practices" or "GMP" means the then-current good manufacturing practices required by the applicable Regulatory Authority, including the MHLW and PMDA or, solely for Akebia's obligations, covenants, and representations under this Agreement, by the FDA.

Section 1.31 "HIF Product" means any product or product candidate that is a hypoxia inducible factor ("HIF") prolyl hydroxylase inhibitor for the treatment of anemia related to

chronic kidney disease. For the avoidance of doubt, "HIF Product" shall include, without limitation, [***] and the Licensed Product.

Section 1.32 "Improvements" Section 1.01 means all Inventions or Know-How relating to, arising from the use of, or including the Licensed Compound or Licensed Product or their respective Development, manufacture, use, design, registration, offer for sale, sale or importation that are made during the Term solely by one or more employees of Licensee or any Affiliate of Licensee, or persons contractually required to assign or license patent rights covering such Inventions to Licensee or any Affiliate of Licensee.

Section 1.33 "IND" means an Investigational New Drug application for submission to the FDA or its equivalent in the Territory.

Section 1.34 "Invention(s)" means any process, method, composition of matter, article of manufacture, discovery or finding that is conceived and/or reduced to practice (whether or not patentable).

Section 1.35 "Joint Inventions" means any Inventions that are jointly made during the Term by at least one (1) employee of Akebia or its Affiliate or person contractually required to assign or license patent rights covering such inventions to Akebia and at least one (1) employee of Licensee or its Affiliate or person contractually required to assign or license patent rights covering such inventions to Licensee.

Section 1.36 "Joint Patents" means all Patents claiming Joint Inventions.

Section 1.37 "Joint Technology" means Joint Inventions and Joint Patents.

Section 1.38 "Know-How" means Inventions, discoveries, trade secrets, information, experience, data, formulas, procedures, technology and results (whether or not patentable), including discoveries, formulae, practices, methods, knowledge, know-how, processes, experience and test data (including physical, chemical, biological, toxicological, pharmacological, clinical and veterinary data), dosage regimens, control assays, product specifications, analytical and quality control data, marketing, pricing, distribution cost and sales data or descriptions.

Section 1.39 "Launch Plan" means the strategic plan for the Licensed Product which details the activities to be conducted prior to launch, plans for launch, and activities to be conducted after launch.

Section 1.40 "Licensee Inventions" means all Inventions that (a) are made during the Term by one or more employees of Licensee or any Affiliate of Licensee, or persons contractually required to assign or license patent rights covering such Inventions to Licensee or any Affiliate of Licensee, and (b) are not Joint Inventions.

Section 1.41 "Licensee Know-How" means all Know-How that is both (a) Controlled as of the Effective Date or during the Term by Licensee or any of its Affiliates in the Territory, and (b) is either (i) [***] or (ii) [***]. For the avoidance of doubt, Licensee Know-How shall include any Know-How developed during pre-clinical or clinical studies conducted by Licensee in the Territory.

Section 1.42 "Licensee Patents" means all Patents (excluding any Joint Patents) that are Controlled as of the Effective Date or during the Term by Licensee or any of its Affiliates.

Section 1.43 "Licensee Reserved Dispute" means any dispute with respect to the [***] and as set forth in the last sentence of Section 1.05 (Akebia Reserved Dispute) hereof.

Section 1.44 "Licensee Technology" means Licensee Know-How and Licensee Patents.

Section 1.45 "Licensee Trademark" means, if the global brand name selected by Akebia for the Licensed Product cannot be used in the Territory pursuant to **Section 6.05** (**Trademarks and International Nonproprietary Name**) hereof, the trademarks approved by the JSC under which Licensee, its Affiliates or its sublicensees will market such Licensed Product in the Territory in the Field, and all trademark registrations and applications therefor, and all goodwill associated therewith.

Section 1.46 "Licensed Compound" means vadadustat, formerly known as AKB-6548.

Section 1.47 "Licensed Product" means any pharmaceutical product, drug product, preparation, formulation, or dosage form that has the Licensed Compound as at least one API.

Section 1.48 "Medical Affairs" means communications with key opinion leaders, medical education, symposia and other medical programs and communications.

Section 1.49 "MHLW" means the Ministry of Health, Labor and Welfare, otherwise referred to as "Koro-Sho," or any successor thereto.

Section 1.50 "NDA" means a New Drug Application or its equivalent for submission to the FDA or its equivalent in the Territory.

Section 1.51 "NDD-CKD Indication" means the treatment of anemia in non-dialysis patients with chronic kidney disease.

Section 1.52 "Net Sales" means the gross invoice price of Licensed Product sold or otherwise transferred to a Third Party by Licensee, its Affiliates or sublicensees (each, a "**Seller**") to independent Third Parties for consideration, reduced by the following amounts to the extent such items are customary under industry practices and to the extent such amounts are included in the gross invoiced sales price:

(a) trade, cash and quantity discounts actually allowed and taken directly with respect to such sales or transfers, and inventory management fees paid to wholesalers and reasonably allocated to such Licensed Product;

(b) tariffs, duties, excises, value added tax and other sales taxes imposed upon and paid with respect to the sale, transportation, delivery, use, exportation, or importation of such Licensed Product (which does not include income, withholding or similar taxes);

(c) amounts actually repaid or credited upon returns, rejections, defects, recalls (due to spoilage, damage, expiration of useful life), price adjustments, billing errors, or trial prescriptions;

(d) invoiced freight, shipping, and insurance expenses specific to the Licensed Product and allocated accordingly;

(e) invoiced amounts that are written off as uncollectible in accordance with Seller's accounting policies, as consistently applied;

(f) allowances or credits to customers on account of price reductions affecting the Licensed Product;

(g) rebates, discounts, or charge-backs actually paid or credited to any governmental agency (or branch of government) or to any Third Party payor, administrator or contractee; and

(h) discounts actually paid under state-legislated or Seller-sponsored discount prescription drug programs or reductions or coupon and voucher programs.

If Seller receives [***] Net Sales for such Licensed Product sold or otherwise transferred.

In the event a Licensed Product is sold as part of a Combination Product, the Net Sales from the Combination Product, for the purposes of determining royalty payments, shall be determined by [***], in each case during the applicable royalty reporting period or, [***]. For purposes of this paragraph, a "**Combination Product**" means any prescription pharmaceutical product which comprises two (2) or more APIs, at least one (1) of which is the Licensed Compound.

If a Licensed Product is sold as part of a Bundled Product, the Seller [***] of the Licensed Product included in such [***]. For purposes of this paragraph, "**Bundled Product**" means products (including one or more Licensed Product) that are either (A) packaged together for sale or shipment as a single unit or sold at a single price or (B) marketed or sold collectively as a single product.

Section 1.53 "Patents" means (a) all patents and patent applications in any country or jurisdiction in the Territory, and (b) any substitutions, divisions, continuations, continuations-in-part, reissues, renewals, registrations, confirmations, re-examinations, extensions, supplementary protection certificates and the like.

Section 1.54 "Phase 1 Trial" means a human clinical trial of a Licensed Product that would satisfy the requirements of 21 C.F.R. Part 312.21(a) (as amended from time to time) or other comparable regulation imposed by an applicable Regulatory Authority in any country other than the United States, the principal purposes of which are to (a) determine the pharmacokinetics, metabolism, and pharmacologic actions of the drug in humans, (b) determine the side effects associated with increasing doses, and (c) if possible, gain early evidence of effectiveness to permit the design of well-controlled, scientifically valid, Phase 2 trials. A Phase 1 Trial shall be deemed initiated upon the enrollment of the first subject.

Section 1.55 "Phase 2 Trial" means a human clinical trial of a Licensed Product that would satisfy the requirements of 21 C.F.R. Part 312.21(b) (as amended from time to time) or other comparable regulation imposed by an applicable Regulatory Authority in any country other than the United States, the principal purposes of which are to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug. A Phase 2 Trial shall be deemed initiated upon the enrollment of the first subject.

Section 1.56 "Phase 3 Trial" means a human clinical trial of a Licensed Product that would satisfy the requirements of 21 C.F.R. Part 312.21(c) (as amended from time to time) or other comparable regulation imposed by an applicable Regulatory Authority in any country other than the United States, the principal purposes of which are to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. A Phase 3 Trial shall be deemed initiated upon the enrollment of the first subject.

Section 1.57 "PMDA" means the Pharmaceuticals and Medical Devices Agency in Japan or any successor thereto, which conducts scientific reviews of marketing authorization application for pharmaceuticals and monitoring of their post-marketing safety in Japan.

Section 1.58 "Regulatory Approval" means, with respect to a particular regulatory jurisdiction, all approvals (other than Reimbursement Approvals), product and/or establishment licenses, registrations or authorizations of any Regulatory Authority necessary for the commercial sale of a Licensed Product in such regulatory jurisdiction.

Section 1.59 "Regulatory Authority" means, in a particular country or jurisdiction, any applicable governmental authority involved in granting Regulatory Approval in such country or jurisdiction, including without limitation (a) in the United States, the FDA and any other applicable governmental authority in the United States having jurisdiction of the Licensed Product, (b) in Europe, the European Medicines Agency ("**EMA**"), and (c) in the Territory, the MHLW, PMDA, and any other applicable governmental authority in the Territory having jurisdiction over the Licensed Product.

Section 1.60 "Regulatory Filings" means all applications, filings, dossiers and the like submitted to a Regulatory Authority for the purpose of obtaining Regulatory Approval from that Regulatory Authority. Regulatory Filings shall include, but not be limited to, all INDs, NDAs and other Regulatory Approval applications and their equivalents in the Territory.

Section 1.61 "Reimbursement Approval" means an approval, agreement, determination, or other decision by the applicable governmental authority and/or Regulatory Authority that establishes prices at which the Licensed Product will be reimbursed by the governmental authorities and/or Regulatory Authorities in the Territory.

Section 1.62 "Safety Data Exchange Agreement" means that agreement regarding receipt, investigation and reporting of product complaints, adverse events, product recalls, and any other information related to the safety of the Licensed Product as set forth in **Section 10.04** (**Adverse Drug Events**) hereof.

Section 1.63 "sNDA" means supplemental New Drug Application or additional application for a previous New Drug Application (for example, seeking approval for a new indication) or its equivalent, for submission to Regulatory Authorities in the Territory.

Section 1.64 "Territory" means Japan, Taiwan, Indonesia, East Timor, South Korea, Mongolia, the Philippines, Vietnam, Laos, Cambodia, Thailand, Malaysia, Singapore, Burney, Myanmar, Nepal, Sri Lanka, Bangladesh, Bhutan, Maldives, Palau, Tonga and India, and their territories and possessions.

Section 1.65 "Third Party" means any person or entity other than a Party or its Affiliates.

Section 1.66 "U.S." means the United States of America.

Section 1.67 "Valid Claim" means a claim in any Akebia Patent in the Territory, which claim has not been held invalid or unenforceable by a non-appealed or un-appealable decision of a court or government agency or other appropriate body of competent jurisdiction and has not been admitted invalid or unenforceable through reissue, reexamination or disclaimer, or has not been made unenforceable due to failure to pay maintenance fees.

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Section 1.68 Interpretation. (a) Whenever any provision of this Agreement uses the term "including" (or "includes"), such term shall be deemed to mean "including without limitation" and "including but not limited to" (or "includes without limitations" and "includes but is not limited to") regardless of whether the words "without limitation" or "but not limited to" actually follow the term "including" (or "includes"); (b) "herein," "hereby," "hereunder," "hereof" and other equivalent words shall refer to this Agreement in its entirety and not solely to the particular portion of this Agreement in which any such word is used; (c) all definitions set forth herein shall be deemed applicable whether the words defined are used herein in the singular or the plural; (d) wherever used herein, any pronoun or pronouns shall be deemed to include both the singular and plural and to cover all genders; (e) the recitals set forth at the start of this Agreement, along with the schedules and the exhibits to this Agreement, and the terms and conditions incorporated in such recitals and schedules and exhibits shall be deemed integral parts of this Agreement and all references in this Agreement to this Agreement shall encompass such recitals and schedules and exhibits and the terms and conditions incorporated in such recitals and schedules and exhibits; *provided*, that in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions set forth in the recitals, schedules or exhibits, the terms of this Agreement shall control; (f) in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions that may be set forth on any order, invoice, verbal agreement or otherwise, the terms and conditions of this Agreement shall govern; (g) this Agreement shall be construed as if both Parties drafted it jointly, and shall not be construed against either Party as principal drafter; (h) unless otherwise provided, all references to Sections, Articles and Schedules in this Agreement are to Sections, Articles and Schedules of and to this Agreement; (i) any reference to any federal, national, state, local or foreign statute or law shall be deemed to also refer to all rules and regulations promulgated thereunder, unless the context requires otherwise; (j) wherever used, the word "shall" and the word "will" are each understood to be imperative or mandatory in nature and are interchangeable with one another; (k) references to a particular person include such person's successors and assigns to the extent not prohibited by this Agreement; (l) references to Akebia's knowledge shall be taken to refer to the knowledge of Akebia's senior management team as of the Effective Date having made no particular inquiry; and (m) the captions used herein are inserted for convenience of reference only and shall not be construed to create obligations, benefits or limitations.

ARTICLE II.

LICENSES

Section 2.01 Grant of License. Subject to the terms and conditions of this Agreement, Akebia hereby grants to Licensee, during the Term;

(i) an exclusive, royalty-bearing license under Akebia Technology and Joint Technology to research, Develop, use, import, offer for sale, and sell the Licensed Compounds and Licensed Products in the Field in the Territory during the Term of this Agreement; and

(ii) a non-exclusive, royalty-bearing license under Akebia Technology and Joint Technology to make and have made the Licensed Compounds and Licensed Products for the purpose of exercising Licensee's foregoing rights (collectively, the "**Licensed Rights**"); *provided, however*, that Licensee may only exercise its right to make and have made Licensed Compounds and Licensed Products in accordance with **Section 7.01** (**Manufacture and Supply of Licensed Products**) hereof.

Section 2.02 Rights to Grant Sublicense. Subject to the terms and conditions of this Agreement, upon Akebia's written consent, not to be unreasonably withheld or delayed, Licensee shall have the right to enter into one or more sublicenses under this Agreement with Third Party/ies to research, Develop, use, make, have made, import, offer for sale, and sell the Licensed Compounds and the Licensed Products in the Field in the Territory during the Term of this Agreement; *provided, however,* that Licensee may only sublicense its right to make and have made Licensed Compounds and Licensed Products in accordance with **Section 7.01** (**Manufacture and Supply of Licensed Products**); *provided further, however*, that Licensee shall have the right to sublicense to its Affiliates without Akebia's consent after providing prior written notification to Akebia identifying Licensee's intention to grant such sublicense, the purpose of such sublicense, and the Affiliate of Licensee to whom Licensee intends to grant such sublicense. All permitted sublicensees shall hold their rights contingent on the Licensed Rights under this Agreement. Any loss by Licensee of its rights under this Agreement due to an early termination of this Agreement for Licensee's breach, pursuant to **Article XIV** (**Term and Termination**), or due to any other reason shall automatically cause all of the permitted sublicensees to lose the same rights under any sublicense. Unless otherwise agreed by Akebia, each sublicense shall require the permitted sublicensee's management to communicate its plan for the Development and Commercialization of the Licensed Product and implement processes for consistent communication and coordination between the sublicensee and Akebia during the term of the sublicense. Licensee agrees that it shall be fully responsible and liable for any breach of the terms of this Agreement by any of its permitted sublicensees to the same extent as if Licensee itself has committed any such breach.

Section 2.03 No Other Rights and Retained Rights. Nothing in this Agreement shall be interpreted to grant Licensee any rights under any Akebia Technology that are not expressly granted herein, whether by implication, estoppel or otherwise. Any rights not expressly granted to Licensee by Akebia under this Agreement are hereby retained by Akebia. For the avoidance of doubt, Akebia retains the right to make, have made, Develop, use, import and export the Licensed Product in the Field in the Territory in order to fulfill its obligations under this Agreement and/or in order to Develop and Commercialize the Licensed Product outside the Territory.

Section 2.04 Knowledge Transfer (a) . Within a reasonable time [***] days following the Effective Date hereof, Akebia shall provide to Licensee an initial onboarding information package describing the Development program for the Licensed Product including, but not limited to, non-clinical and clinical data, intellectual property and associated information, regulatory information and market research. Akebia shall make its qualified personnel reasonably available to Licensee, free of charge to Licensee, at Akebia's place of business and upon reasonable prior notice for the purpose of discussing such information under this **Section 2.04** (**Knowledge Transfer**). All further requests for additional information will be addressed through the Alliance Managers.

ARTICLE III.

GOVERNANCE

Section 3.01 Formation and Purpose of JSC. Within thirty (30) days after the Effective Date, Licensee and Akebia shall establish the Joint Steering Committee ("**JSC**"), which shall consist of [***] members, shall coordinate the Parties' activities hereunder and shall have the additional responsibilities provided for herein. The JSC will establish a charter that will include details regarding the operation of the JSC consistent with **Article III** (**Governance**) hereof. The JSC will dissolve upon the expiration of the Term.

Section 3.02 Membership. Each Party shall designate [***] representatives with appropriate knowledge and expertise to serve as members of the JSC. Each Party may replace its JSC representatives at any time upon written notice to the other Party. Akebia may designate one (1) of its JSC members as the co-chairperson and Licensee may designate one (1) of its JSC members as the co-chairperson. [***] "**Lead Co-Chairperson**". The Lead Co-Chairperson shall be responsible for calling meetings, preparing and circulating an agenda in advance of each meeting, and preparing and issuing minutes of each meeting within thirty (30) days thereafter. Such minutes will not be finalized until all JSC members have had an adequate opportunity to review and confirm the accuracy of such minutes in writing.

Section 3.03 Meetings. The JSC shall hold meetings at such times as it elects to do so, but in no event shall such meetings be held less frequently than twice a year. The JSC shall meet alternatively at Licensee's facilities in Tokyo, Japan and Akebia's facilities in Cambridge, Massachusetts, or at such locations as the Parties may otherwise agree. Other employees of each Party (including without limitation, the Alliance Managers of each Party) involved in the Development or Commercialization of Licensed Product may attend meetings of the JSC as non-voting participants, and, with the consent of each Party, consultants, representatives, or advisors involved in the same activities may attend meetings of the JSC as non-voting observers; *provided*, *however*, that such Third Party participants and observers are under obligations of confidentiality and non-use applicable to the Confidential Information of each Party and that are at least as stringent as those set forth in **Article XII** (**Confidentiality**). Each Party shall be responsible for all of its own expenses of participating in any JSC meeting. Meetings of the JSC may be held by audio or video teleconference with the consent of each Party; *provided*, *however*, that at least one (1) JSC meeting per year shall be held in person.

Section 3.04 Decision Making and JSC Dispute Resolution. Each Party's representatives on the JSC shall, collectively, have one (1) vote (the "**Party Vote**") on all matters brought before the JSC. The JSC shall operate as to matters within its jurisdiction by [***]; *provided*, *however*, that the JSC shall not have the authority to amend or modify, or waive compliance with, this Agreement. Any disagreement between the representatives of Licensee and Akebia on JSC matters within the JSC's jurisdiction shall, at the election of either Party, be referred for resolution pursuant to **Article XV** (**Dispute Resolution, Governing Law**).

Section 3.05 Meeting Agendas. Each Party shall disclose to the other Party the proposed agenda items along with appropriate information at least [***] Business Days in advance of each meeting of the JSC; *provided* that under exigent circumstances requiring JSC input, a Party may provide its agenda items to the other Party within a lesser period of time in advance of the meeting, or may propose that there not be a specific agenda for a particular meeting, so long as such other Party consents to such later addition of such agenda items or the absence of a specific agenda for such JSC meeting.

Section 3.06 Additional Committees. The JSC shall establish and delegate duties to other committees or ad-hoc sub-committees, including a Development committee and a

Commercialization committee (each a "**Sub-Committee**"), on an as needed basis to oversee particular projects or activities. Each such Sub-Committee shall be constituted and shall operate as the JSC determines and shall be co-chaired by the Alliance Managers. Each Sub-Committee and its activities shall be subject to the oversight, review and approval of, and shall report to, the JSC. The authority of the Sub-Committee cannot exceed that specified for the JSC in this **Article III** (**Governance**).

Section 3.07 Interactions Between Committees and Internal Teams. The Parties recognize that while they will establish the JSC and Sub-Committees under this Agreement, each Party possesses an internal structure (including without limitation various committees, teams and review boards) that will be involved in administering such Party's activities under this Agreement. If requested by a Party, the JSC and Sub-Committees shall establish procedures to facilitate communications between the JSC or such Sub-Committee and the relevant internal committee, team or board of the requesting Party. Such procedures may include, to the extent reasonably necessary, requiring appropriate members of the JSC or Sub-Committee to be available at reasonable times and places and upon reasonable prior notice for making appropriate reports to, and responding to reasonable inquiries from, the relevant internal committee, team or board.

Section 3.08 Specific Responsibilities of the JSC. In addition to its overall responsibility under this Agreement for the Development and Commercialization of Licensed Compounds and Licensed Products, the JSC shall, in particular:

(a) coordinate the activities of the Parties hereunder;

(b) resolve any disputes or disagreements, including those arising from any Sub-Committee, or submit unresolved disputes or disagreements to the designated executive officers pursuant to **Section 3.04** (**Decision Making and JSC Dispute Resolution**) and **Article XV** (**Dispute Resolution, Governing Law**);

(c) support Development and Commercialization efforts for Licensed Compounds and Licensed Products, including reviewing and discussing the strategy for the Development and Commercialization of Licensed Compounds and Licensed Products;

(d) make recommendations for approval by the Parties for [***] programs;

(e) subject to **Section 4.02** (**Development Plan**), review and approve the Development Plan [***];

(f) review and approve any Development in the Territory for [***] of the DD-CKD Indication and NDD-CKD Indication;

(g) subject to **Section 6.05** (**Trademarks and International Nonproprietary Name**), review and discuss the use in the Territory of the [***] for the Licensed Product, which shall be prepared by Akebia, and review and discuss the [***] for each country in the Territory, which shall be prepared by Licensee;

(h) review and discuss a [***] including supporting materials for a [***] for [***] taking into consideration [***] for the [***];

(i) review commercial and sales performance, and sales forecasts, of the Licensed Product in each country in the Territory; and

(j) perform such other functions as appropriate to further the purposes of this Agreement as determined by the Parties, including the periodic evaluation of performance against goals.

Section 3.09 Alliance Managers. Each of the Parties shall appoint a single individual to manage Development and Commercialization obligations between the Parties (each, an "**Alliance Manager**"). The role of the Alliance Manager is to act as a single point of contact between the Parties to ensure a successful relationship under this Agreement. The Alliance Managers may attend all JSC meetings and support their co-chairperson of the JSC in the discharge of his/her responsibilities. Alliance Managers shall be non-voting participants in such JSC meetings, unless they are also appointed members of the JSC; *provided*, *however*, that an Alliance Manager may bring any matter to the attention of the JSC if such Alliance Manager reasonably believes that such matter warrants such attention. Each Party may change its designated Alliance Manager at any time upon written notice to the other Party. Any Alliance Manager may designate a substitute to temporarily perform the functions of that Alliance Manager by written notice to the other Party. Each Alliance Manager will also: (i) be the point of first referral in all matters of conflict resolution; (ii) provide a single point of communication for seeking consensus between the Parties regarding key strategy and plan issues; (iii) identify and bring disputes to the attention of the JSC in a timely manner; (iv) plan and coordinate cooperative efforts and internal and external communications; (v) co-chair any Sub-Committees established by the JSC pursuant to **Section 3.06** (**Additional Committees**) hereof; and (vi) take responsibility for ensuring that governance activities, such as the conduct of required JSC meetings and production of meeting minutes, occur as set forth in this Agreement, and the relevant action items resulting from such meetings are appropriately carried out or otherwise addressed.

ARTICLE IV.

DEVELOPMENT

Section 4.01 Development in the Territory.

(a) Clinical Development in Japan. The Parties intend to use Commercially Reasonable Efforts to include [***] for the [***] based on the [***]. In the event that [***] associated with the [***] as set forth in the Development Plan, subject to **Section 5.01** (**Regulatory Filings**) hereof, and [***]. Without affecting the generality of the foregoing, if either Party becomes aware of an event which would cause a material adverse effect to proceeding with the [***], such Party shall promptly notify the other Party and the Parties shall promptly discuss potential solutions, including that Licensee conducts certain supporting activities of the [***] subject to the approval of JSC. In the event that [***], Licensee shall be responsible for the [***].

(b) Clinical Development in Countries in the Territory Other Than Japan. Licensee shall be responsible for the Development of Licensed Compounds and Licensed Products in all countries in the Territory other than Japan and all costs associated therewith; *provided, however,* that if any such country is [***]. For the avoidance of doubt, Licensee shall be responsible for all other Development in such country.

(c) Non-Clinical Development in the Territory. For the avoidance of doubt, Licensee shall be solely responsible for all non-clinical Development that is specific to a country in the Territory other than non-clinical activities conducted by Akebia to support approval outside the Territory which will be made available to Licensee pursuant to **Section 5.01(b)** hereof; [***]. Licensee shall have the right to request that Akebia conduct any other non-clinical studies

required for the Territory, subject to reimbursement by Licensee of Akebia's internal and external costs associated with such non-clinical studies.

Section 4.02 Development Plan. The Party responsible for Development in a country in the Territory pursuant to **Section 4.01** (**Development in the Territory**) (the "**Developing Party**"), with the cooperation, support and assistance of the other Party, will prepare the initial Development Plans for such country in the Territory within [***] days of the Effective Date, to be submitted to the JSC. The JSC will review and approve the initial Development Plan within [***] days of receipt. The Developing Party will be responsible for preparing subsequent amendments to the Development Plan, which shall be submitted to the JSC for approval.

Section 4.03 Development Reports. Within [***] Business Days after the end of each calendar quarter, the Developing Party shall, through the JSC, provide the other Party with a written report that summarizes Development in each country in the Territory performed by the Developing Party, its Affiliates or any sublicensee during the prior calendar quarter, which report shall include the status of each pending and proposed Regulatory Filing for Licensed Products in the Territory. In addition, the Developing Party shall promptly provide written notice, through the JSC or Alliance Managers, to the other Party of any significant Development events (*e.g.*, clinical trial initiation or completion, clinical holds, Regulatory Filings for the Licensed Product, Regulatory Approvals, or Clinical Data, which, in any case, is significant).

Section 4.04 Standards of Conduct. Akebia and Licensee shall perform, and shall ensure that its Affiliates, permitted sublicensees and Third Party contractors perform, all Development activities under the Development Plan in a good scientific manner, in accordance with GLP and GCP, as applicable, and in compliance in all material respects with applicable laws, rules and regulations.

Section 4.05 Developmental Efforts. Each Party, directly or through its Affiliates, permitted sublicensees and Third Party contractors, shall use Commercially Reasonable Efforts to Develop, or support the Development of, Licensed Compounds and Licensed Products in the Territory. For the avoidance of doubt, each Party shall be permitted to use Third Party contractors to perform its Development obligations hereunder, subject to the terms and conditions of this Agreement.

Section 4.06 Records. Licensee and its Affiliates and permitted sublicensees shall maintain written or electronic records in sufficient detail, in a good scientific manner (in accordance with GLP, GCP and GMP, as applicable) and appropriate for regulatory and patent purposes, which are complete and accurate in all material respects and reflect all Development work performed under the Development Plan and results achieved.

Section 4.07 Medical Affairs. Licensee shall be responsible for Medical Affairs in the Territory, with Akebia's cooperation, support and assistance.

ARTICLE V.

REGULATORY

Section 5.01 Regulatory Filings.

(a) Under the oversight of the JSC and subject to **Section 4.02** (**Development Plan**), Licensee shall be responsible for preparing and filing, directly or through its Affiliates and permitted sublicensees, all Regulatory Filings and seeking all Regulatory Approvals in the Territory; *provided, however*, that, unless otherwise agreed upon by the Parties, (i) Akebia shall be responsible for [***], (ii) Licensee shall be responsible for [***] and (iii) the JSC will

determine the Parties' responsibilities for any other Regulatory Filings related to the Global Phase 3 Program in the Territory. Licensee shall provide Akebia with copies of such draft Regulatory Filings reasonably in advance of filing so that Akebia may review, comment and approve such Regulatory Filings. Except as otherwise provided in this **Section 5.01(a)**, all Regulatory Filings for Licensed Products in the Territory shall be filed in the name of Licensee (or its Affiliates or permitted sublicensees) and Licensee shall be responsible for all communications and other dealings with the Regulatory Authorities relating to the Licensed Product in the Territory; *provided*, *however*, that representatives of Akebia will be invited to attend all meetings, and copied on all written correspondence, with Regulatory Authorities in the Territory. All Regulatory Filings and Regulatory Approvals in the Territory shall be at Licensee's sole expense.

(b) In support of Licensee's preparation and filing of any IND equivalent, amendment thereto, or NDA with respect to any Licensed Product in the Territory, Akebia shall provide Licensee access to a complete electronic copy of all relevant documentation submitted by Akebia to the FDA or EMA that would be necessary or useful to Licensee in preparing its own IND or NDA for a particular Licensed Product for use in the Territory (collectively, the "**Akebia Regulatory Documents**"). In support of Akebia's (or its Affiliates or sublicensees) preparation and filing of any IND equivalent, amendment thereto, or NDA with respect to any Licensed Product outside of the Territory, Licensee shall provide Akebia access to a complete electronic copy of all relevant documentation submitted by Licensee to Regulatory Authorities in the Territory that would be necessary or useful to Akebia in preparing its own IND or NDA for a particular Licensed Product for use outside the Territory (collectively, the "**Licensee Regulatory Documents**"). Each Party shall make available to the other Party copies of any other documentation related to the Licensed Compound or Licensed Product, including but not limited to research data and reports, material regulatory materials and correspondence (including INDs and NDAs), clinical and preclinical data, and chemistry, manufacturing and controls ("**CMC**") data (collectively, the "**Clinical Data**") if such Clinical Data is necessary for Licensee to conduct clinical studies and/or obtain Regulatory Approval in the Territory or for Akebia to conduct clinical studies and/or obtain Regulatory Approval outside of the Territory. Licensee and its Affiliates and permitted sublicensees shall be entitled at no cost to access, use, and reference the Akebia Regulatory Documents and Clinical Data for the Development and Commercialization of the Licensed Compound or Licensed Product in the Territory. Akebia and its Affiliates and sublicensees shall be entitled at no cost to access, use, and reference the Licensee Regulatory Documents and Clinical Data for the Development and Commercialization of the Licensed Compound or Licensed Product outside of the Territory. All Regulatory Documents and Clinical Data shall be considered Confidential Information pursuant to **Article XII** (**Confidentiality**) hereof.

ARTICLE VI.

COMMERCIALIZATION

Section 6.01 General. Under the direction of the JSC, Licensee, its Affiliates and permitted sublicensees shall be solely responsible for the Commercialization of the Licensed Product in the Territory. Licensee, its Affiliates and permitted sublicensees shall be responsible for all costs associated with the Commercialization of Licensed Product. Licensee shall prepare a Launch Plan, which shall be reviewed and approved by the JSC no later than [***] after filing the first NDA in the Territory, and an annual Commercialization Plan, which shall be [***] by the JSC no later than [***] following Regulatory Approval of the Licensed Product and annually thereafter. The Launch Plan shall be a strategic, high-level plan and shall include, without limitation, launch budgets. The Commercialization Plan shall include, without limitation, the following elements:

(a) [***] of the Licensed Product by Licensee's sales representatives during the [***] after First Commercial Sale of the Licensed Product;

(b) [***] who market and sell the Licensed Products;

(c) sales forecasts for the Licensed Products; and

(d) Commercialization budgets.

The Parties shall share their promotional materials for the Licensed Product on a regular basis, and Akebia shall have the right to review such promotional materials prior to their use in the Territory.

Section 6.02 Commercialization Reports. Within [***] Business Days after the end of each calendar quarter following the First Commercial Sale, Licensee shall provide Akebia with (i) a written report that summarizes Commercialization activities performed during the prior calendar quarter, (ii) detailed sales reports for the Licensed Product for each month of the prior calendar quarter in each country in the Territory, and (iii) quarterly sales forecasts for the Licensed Products in each country in the Territory.

Section 6.03 Commercialization Efforts. Licensee, directly or through its Affiliates and/or permitted sublicensees, shall use Commercially Reasonable Efforts to obtain Regulatory Approval and Reimbursement Approval in the Territory and thereafter to Commercialize the Licensed Product in the Territory.

Section 6.04 Standards of Conduct. Licensee shall perform, or shall ensure that its Affiliates, permitted sublicensees and Third Party contractors perform, all Commercialization activities in a professional and ethical business manner and in compliance in all material respects with applicable laws, rules and regulations.

Section 6.05 Trademarks and International Nonproprietary Name. Licensee shall Commercialize the Licensed Product under the Akebia Trademarks using the global brand name for the Licensed Product selected by Akebia unless prohibited by applicable laws or for other reasons specific to a country in the Territory (*e.g.*, cultural and linguistic differences, varying business practices). In addition, Akebia will reasonably consider Licensee's comments regarding the use of the global brand name in each country in the Territory, however, Akebia will make the final decision in its sole discretion whether to use the global brand name for the Licensed Product in such country. If Akebia ultimately determines that the global brand name is not appropriate for use in a particular country, the JSC shall approve an alternative brand name for the Licensed Product for use in that country in the Territory and such brand name shall be a Licensee Trademark. Akebia will be responsible for the selection and filing of the international nonproprietary name for any Licensed Product or Licensed Compound with the World Health Organization and any Regulatory Authorities in the Territory, which Licensee shall have the right to reference.

ARTICLE VII.

MANUFACTURING AND SUPPLY

Section 7.01 Manufacture and Supply of Licensed Products.

(a) Subject to the terms and conditions of this Agreement, Akebia shall be responsible for manufacturing or having manufactured and supplying all reasonable requirements of Licensed Product for clinical and commercial use in the Territory in accordance with GCP and

GMP at the same level of diligence [***]. If necessary, the Parties shall agree upon a supply agreement for the clinical supply of the Licensed Product by Akebia to Licensee in the Territory pursuant to which Akebia shall supply Licensed Products at [***]. Prior to commercial launch of the Licensed Product, the Parties shall agree upon a supply agreement for the commercial supply of the Licensed Product by Akebia to Licensee in the Territory, which shall include provisions regarding long-range forecasting of Licensee's requirements for the Licensed Product. Promptly after the execution of a supply agreement, the Parties will enter into a mutually acceptable quality agreement, which shall include the Parties' respective obligations and responsibilities relating to quality assurance requirements for Licensed Products.

(b) After First Commercial Sale of the Licensed Product in the Territory, Licensee shall have the right, but not the obligation, [***]; *provided*, *however*, that if Licensee chooses to exercise its [***] it shall also [***]. If Licensee wishes to exercise this right, it shall so notify Akebia, and [***]. For the avoidance of doubt, Licensee shall not be permitted to [***]. Upon the execution of a [***], which shall include the Parties' respective obligations and responsibilities relating to matters of [***]. If Licensee wishes to [***] pursuant to this **Section 7.01(b)**, Licensee may do so only with Akebia's prior written consent, not to be unreasonably withheld or delayed, and all other terms of this **Section 7.01(b)** shall apply.

(c) If, at any time during the Term, Licensee reasonably expects that Akebia will be [***], Licensee may request a discussion with Akebia and the Parties shall promptly discuss a potential resolution, which may include a [***].

Section 7.02 Supply Price. The supply price for Licensed Products supplied by Akebia to Licensee for commercial use will be equal to [***] (the "**Supply Price**").

Section 7.03 Labeling. Licensed Products shall bear Licensee's name and Akebia's company name on the labels, containers, cartons, package inserts and other packaging and labeling to the extent practicable and permitted by applicable laws. Akebia hereby grants Licensee a fully-paid, non-exclusive license under Akebia's Trademarks as necessary to effect the co-labeling provided for in this Agreement and to Develop and Commercialize Licensed Products in the Territory. Licensee shall be responsible for packaging and labeling Licensed Products for use in the Territory and for all costs associated therewith.

ARTICLE VIII.

PAYMENTS

Section 8.01 Upfront License Fee. As consideration for the rights and licenses granted by Akebia to Licensee under this Agreement, within fifteen (15) Business Days of the Effective Date, and provided that Licensee is in receipt of Akebia's Certificate of Residency from the U.S. Department of Treasury ("**Form 6166**"), and Application Form for Income Tax Convention ("**Form 3**"), and Attachment Form for Limitation on Benefits Article ("**Form 17**") from the Japanese National Tax Agency (collectively, the "**Tax Forms**"), Licensee shall pay Akebia a nonrefundable, noncreditable upfront license fee of [***]. If Licensee is not in receipt of Akebia's Tax Forms within fifteen (15) Business Days of the Effective Date, then the upfront license fee shall be paid by Licensee within fifteen (15) Business Days following receipt of Akebia's Tax Forms.

Section 8.02 Development Costs.

(a) In the [***], in addition to being responsible for all Development costs for Licensed Products in the Territory outside of Japan pursuant to **Section 4.01** (**Development in the Territory**), Licensee shall be responsible for (i) up to [***] of the total internal and external

Development costs associated with Development in the Global Phase 3 Program, including the Global Phase 3 DD-CKD Study and the Global Phase 3 NDD-CKD Study, and (ii) all internal and external Development costs associated with any additional clinical studies performed in the Territory used to obtain Regulatory Approval of the Licensed Product in the Territory, as defined in the initial Development Plan to be approved by the Parties, *provided, however,* that Licensee's responsibility for Development costs in the [***] shall not exceed [***].

(b) In the event that [***], then Licensee shall be responsible for (i) up to [***] of the Global Phase 3 Program costs associated with such indication based on the Development Plan approved by the JSC, and (ii) all internal and external Development costs associated with any additional clinical studies performed in the Territory to support Regulatory Approval of the Licensed Product for such indication in the Territory, up to a maximum amount of [***]. For the avoidance of doubt, Licensee shall be solely responsible for [***].

(c) [***], the Parties shall discuss in good faith, and include in the Development Plan, the consideration to be paid by Licensee for use of, or reference to, [***].

(d) Akebia will invoice Licensee for such costs as incurred in accordance with the budgets and payment schedules for such Development costs which will be included in the JSC-approved Development Plan for the Global Phase 3 Program. Upon the receipt of an undisputed invoice from Akebia with sufficient details and documentation of incurred costs, Licensee shall make a payment to Akebia within forty-five (45) days pursuant to the invoice.

(e) Within fifteen (15) Business Days after the Effective Date, Licensee shall pay Akebia a pre-payment for Development costs in the amount of [***] ("**Development Cost Pre-Payment**"). The Development Cost Pre-Payment shall be deducted from the total amount payable by Licensee in accordance with **Section 8.02(a)** and **Section 8.02(b)** hereof. In the event that, ultimately, neither **Section 8.02(a)** nor **Section 8.02(b)** hereof is applied, then Akebia shall, at Licensee's discretion and within [***] days of Licensee's request, either (i) [***] or (ii) [***]. If Licensee is not in receipt of Akebia's Tax Forms within fifteen (15) Business Days after the Effective Date, then the Development Cost Pre-Payment shall be paid by Licensee within fifteen (15) Business Days following receipt of Akebia's Tax Forms.

Section 8.03 Milestone Payments. Licensee shall pay to Akebia the following non-refundable and non-creditable amounts no later than [***] days after the first occurrence of the indicated event for the Licensed Product:

Development Milestones

Event	Payment Amount (in U.S. Dollars)
[***]	[***]
[***]	[***]
[***]	*In the [***]:* · [***] · [***] *In the [***]:* · [***] *In the event that Licensee determines, in its sole discretion, to [***], Licensee shall pay Akebia [***] of the above milestone payments for the [***] for the Licensed Product and [***] of the above milestones for the [***] for the Licensed Product.*
[***]	*In the [***]:* · [***] · [***], in which case the milestone payment shall be [***]. *In the [***]*: [***] *In the event that Licensee determines, in its sole discretion, to [***], Licensee shall pay Akebia [***] of the above milestone payments for Regulatory Approval of the Licensed Product for [***] and [***] of the above milestone payments for Regulatory Approval of the Licensed Product for [***].*
[***]	[***]
[***]	[***]

Sales Milestones

Event	Payment Amount (in U.S. Dollars)
Achievement of [***] of aggregate annual Net Sales of Licensed Products in the Territory	[***]
Achievement of [***] in aggregate annual Net Sales of Licensed Products in the Territory	[***]
Achievement of [***] in aggregate annual Net Sales of Licensed Products in the Territory	[***]

Each milestone payment shall be paid upon the first occurrence of the event in the Territory and Licensee shall not be obligated to pay each milestone payment more than once unless otherwise indicated.

Section 8.04 Royalties

(a) Licensee shall pay Akebia the following royalties on Net Sales, at an incremental royalty rate determined by aggregate annual Net Sales of each Licensed Product in each calendar year during the Term of this Agreement in the Territory:

Portion of Annual Net Sales	Royalty
Less than [***] Japanese Yen	[***]
[***] Japanese Yen	[***]
Greater than [***] Japanese Yen	[***]

(b) Running royalties paid by Licensee under **Section 8.04** (**Royalties**) shall be paid on a country-by-country basis from the date of the First Commercial Sale of Licensed Product in a country in the Territory until the later of (i) expiration of the last-to-expire Valid Claim that would, but for the licenses granted hereunder, be infringed by the making, using, selling or importing of such Licensed Product in such country in the Territory, (ii) expiration of marketing or regulatory exclusivity in such country in the Territory, or (iii) if no Valid Claim exists in such country in the Territory, then for ten (10) years from the First Commercial Sale of Licensed Product in such country in the Territory (the "**Royalty Term**").

(c) If (i) one or more Generic Products to a Licensed Product is, or are, commercially available in any country in the Territory during the Royalty Term for such Licensed Product in such country, and (ii) Net Sales of such Licensed Product in such country during a calendar quarter decline by [***], as compared with the average Net Sales of such Licensed Product in such country for [***] immediately preceding the calendar quarter in which the first Generic Product is launched in such country, the amount of Net Sales to be utilized for the calculation of royalties provided in **Section 8.04** (**Royalties**) for such Licensed Product shall be reduced in such country by [***] for the calendar quarter in which the applicable decline occurs and for all future calendar quarters.

(d) For the purpose of this paragraph, "**Generic Product**" means, with respect to a Licensed Product in a particular country, any pharmaceutical product that (A)(1) contains at least one of the same API as such Licensed Product and is approved by the Regulatory Authority in such country for an indication for which such Licensed Product obtained Regulatory Approval from the applicable Regulatory Authority in such jurisdiction; or (2) is approved by the Regulatory Authority in such country as a substitutable generic for such Licensed Product, for an indication for which such Licensed Product obtained Regulatory Approval from the applicable Regulatory Authority in such country, on an expedited or abbreviated basis in a manner that relied on or incorporated data submitted by Licensee or its Affiliate or sublicensee in connection with the Regulatory Approval for the Licensed Product in such jurisdiction; and (B) is sold in such country by a Third Party that is not a sublicensee of Licensee and did not purchase such product in a chain of distribution that included Licensee or its Affiliates or any sublicensees of Licensee.

Section 8.05 Royalty Payments and Reports.

(a) Until the expiration of the Royalty Term, Licensee agrees to provide quarterly written reports to Akebia within [***] days after the end of each calendar quarter, covering all Net Sales of the Licensed Product in the Territory by Licensee, its Affiliates or permitted sublicensees, each such written report stating for the period in question:

(i) the quantity and description of Licensed Product sold during the calendar quarter in the Territory, and

(ii) the calculation of Net Sales in the Territory for such quarter and year-to-date Net Sales in the Territory, and

(iii) the exchange rates used to calculate the royalties payable in U.S. Dollars, and

(iv) any withholding taxes required to be made from such royalties.

(b) The information contained in each report under **Section 8.05** (**Royalty Payments and Reports**) shall be considered Confidential Information of Licensee. [***] days after the end of each calendar quarter, Licensee shall make the royalty payment due hereunder for the calendar quarter covered by such report.

Section 8.06 Accounting

(a) Licensee shall keep full, clear and accurate records in accordance with Japanese generally accepted accounting principles (if Licensee starts to apply International Financial Reporting Standards (IFRS) to its accounting, IFRS will be applied) consistently applied for a period of at least three (3) years after the relevant payment is owed pursuant to this Agreement, setting forth the sales of Licensed Product in sufficient detail to enable royalties and compensation payable to Akebia hereunder to be determined. Licensee further agrees to permit its books and records to be examined by an independent accounting firm selected by Akebia to verify reports provided for in **Section 8.05** (**Royalty Payments and Reports**). Such audit shall not be performed more frequently than once per calendar year. Such examination is to be made at the expense of Akebia, except in the event that the results of the audit reveal an underpayment by Licensee of five percent (5%) or more during the period being audited, in which case reasonable audit fees for such examination shall be paid by Licensee.

(b) Akebia shall keep full, clear and accurate records in accordance with U.S. GAAP consistently applied for a period of at least three (3) years after the relevant payment is made by Licensee to Akebia pursuant to this Agreement. Akebia further agrees to permit its books and records to be examined by an independent accounting firm selected by Licensee to verify the accuracy of Development costs for the Global Phase 3 Program and COGS. Such audit shall not be performed more frequently than once per calendar year. Such examination is to be made at the expense of Licensee, except in the event that the results of the audit reveal an overcharge by Akebia of five percent (5%) or more over the period being audited, in which case reasonable audit fees for such examination shall be paid by Akebia.

Section 8.07 Currency Conversion. Wherever it is necessary to convert currencies for Net Sales invoiced in a currency other than the U.S. Dollar, including Japanese Yen, such conversion shall be made into U.S. Dollars after being converted at the rate of Telegraph Transfer Middle Rate announced by The Bank of Tokyo-Mitsubishi UFJ, Ltd. on the last Business Day of the reporting calendar quarter.

Section 8.08 Methods of Payment. All payments due to Akebia under this Agreement shall be made in U.S. Dollars by wire transfer to a bank account of Akebia designated from time to time in writing by Akebia.

Section 8.09 Taxes. Akebia will pay any and all taxes levied on account of any payments made to it under this Agreement. If, under any law or regulation of any country of the Territory, withholding of taxes of any type, levies or other charges is required with respect to any amounts payable hereunder to a Party, the other Party ("**Withholding Party**") shall apply the withholding or deduction as so required and shall promptly pay such tax, levy or charge to the proper governmental authority, and shall promptly furnish the Party with proof of such payment. The Withholding Party shall have the right to withhold or deduct any such tax, levy or charge actually paid from payment due to the Party or be promptly reimbursed by the Party if no further payments are due the Party. Any amounts so withheld or deducted from the payment due the Party pursuant to the relevant law or regulation shall be deemed paid to such Party for all purposes of this Agreement. Each Withholding Party agrees to assist the other Party in claiming

exemption from (or reduction in) such deductions or withholdings under double taxation or similar agreement or treaty from time to time in force and in minimizing the amount required to be so withheld or deducted. Notwithstanding the foregoing, all sums payable by either Party pursuant to this Agreement are stated exclusive of any sales tax, value added tax or other similar taxes, assessments and charges imposed by the jurisdiction of the Withholding Party or the payee and any such taxes shall be paid by the Withholding Party. Notwithstanding anything contrary to the foregoing, at the beginning of each calendar year during the Term, Akebia shall provide Licensee with Akebia's Tax Forms together with any other documents required to be submitted to respective tax authorities for avoiding withholding taxes applicable to any payments to be paid to Akebia from Licensee (the "**Withholding Tax Avoiding Documents**"). If Akebia fails to provide Licensee with the Withholding Tax Avoiding Documents at the beginning of each calendar year, until Akebia provides all of the Withholding Tax Avoiding Documents to Licensee, Licensee may [***].

Section 8.10 Late Payments. Any amount owed by Licensee to Akebia under this Agreement that is not paid within the applicable time period set forth herein shall accrue interest at the lesser of (a) the London Interbank Offered Rate plus three percent (3%) or (b) the highest rate permitted under applicable law.

ARTICLE IX.

OWNERSHIP OF INTELLECTUAL PROPERTY

Section 9.01 Akebia Intellectual Property. Ownership of the Akebia Inventions, Akebia Know-How, and Akebia Patents (other than Joint Patents), shall remain vested at all times in Akebia.

Section 9.02 Licensee Intellectual Property. Ownership of the Licensee Inventions, Licensee Know-How, Improvements, and Licensee Patents (other than Joint Patents) shall remain vested at all times in Licensee.

Section 9.03 Joint Technology and Improvements

(a) The Parties shall promptly disclose to each other any Joint Inventions or Improvements conceived or reduced to practice, but no later than thirty (30) days after such conception or reduction to practice.

(b) Ownership of Joint Technology shall be vested jointly in Akebia and Licensee. Licensee hereby grants to Akebia (i) the exclusive, royalty-free, sublicensable, irrevocable right and license to practice, make, have made, use, import, offer for sale or sell any Improvements and Joint Technology outside of the Territory as is necessary in connection with the Development or Commercialization of the Licensed Compound or the Licensed Product; and (ii) the non-exclusive, royalty-free, sublicensable, irrevocable right and license to practice, make, have made, use, import, offer for sale or sell any Improvements and Joint Technology inside the Territory as is necessary for Akebia to perform its obligations under this Agreement.

(c) Licensee hereby grants to Akebia (i) the exclusive, royalty-free, sublicensable, irrevocable right and license to practice, make, have made, use, import, offer for sale or sell any Improvements and Joint Technology relating solely to the Licensed Compound or Licensed Product for any purpose outside of the Territory; and (ii) the non-exclusive, royalty-free, sublicensable, irrevocable right and license to practice, make, have made, use, import, offer for sale or sell all other Improvements and Joint Technology for any purpose outside of the Territory. During the Term of this Agreement, Licensee [***] without Akebia's written consent, not to be unreasonably withheld or delayed.

Section 9.04 Prosecution of Akebia Patents

(a) Akebia shall have the first right, but not the obligation, to prosecute and maintain the Akebia Patents. On a semiannual basis, Akebia shall provide to Licensee a written summary of the status of all Akebia Patents, including patent applications within Akebia Patents in the Territory. On the reasonable request of Akebia, Licensee shall cooperate with Akebia in connection with the prosecution of all patent applications included within Akebia Patents.

(b) Licensee undertakes without cost to Akebia to obtain all necessary assignment documents for Akebia, to render all signatures that shall be necessary for such patent filings and to assist Akebia in all other reasonable ways that are necessary for the issuance of the patents involved as well as for the maintenance and prosecution of such patents. Akebia shall be responsible for [***] of the costs incurred with respect to the prosecution and maintenance of such Akebia Patents.

(c) Should Akebia decide that it is no longer interested in maintaining or prosecuting a particular Akebia Patent in the Territory during the Term, it shall promptly advise Licensee of this decision. Licensee may, upon written notice to Akebia, assume such prosecution and maintenance at its sole expense. Akebia shall assign such Akebia Patent to Licensee at no cost to Licensee. Following such assignment, such patent or patent application shall no longer be considered an Akebia Patent and shall be considered a Licensee Patent.

Section 9.05 Prosecution of Licensee Patents Covering Improvements

(a) Licensee shall have the first right, but not the obligation, to prosecute and maintain the Licensee Patents that cover Improvements. On a semiannual basis, Licensee shall provide to Akebia a written summary of the status of all Licensee Patents that cover Improvements, including patent applications within Licensee Patents that cover Improvements. On the reasonable request of Licensee, Akebia shall cooperate with Licensee in connection with the prosecution of all patent applications included within Licensee Patents that cover Improvements.

(b) Akebia undertakes without cost to Licensee to obtain all necessary assignment documents for Licensee, to render all signatures that shall be necessary for such patent filings and to assist Licensee in all other reasonable ways that are necessary for the issuance of the patents involved as well as for the maintenance and prosecution of such patents. Licensee shall be responsible for [***] of the costs incurred with respect to the prosecution and maintenance of such Licensee Patents that include Improvements.

(c) Should Licensee decide that it is no longer interested in maintaining or prosecuting a particular Licensee Patent that covers Improvements during the Term, it shall promptly advise Akebia of this decision. Akebia may, upon written notice to Licensee, assume such prosecution and maintenance at its sole expense. Licensee shall assign such Licensee Patent that covers Improvements to Akebia at no cost to Akebia. Following such assignment, such patent or patent application shall no longer be considered a Licensee Patent and shall be considered an Akebia Patent.

Section 9.06 Prosecution of Joint Patents

(a) Akebia will have the first right of election to file patent applications for Joint Inventions. If Akebia declines to file such applications then Licensee may do so. On a semi-annual basis, Akebia shall provide to Licensee a written summary of the status of all Akebia Patents, including patent applications within Akebia Patents in the Territory. On the reasonable request of Akebia, Licensee shall cooperate with Akebia in connection with the prosecution of all patent applications included within Joint Patents.

(b) Licensee undertakes without cost to Akebia to obtain all necessary assignment documents for Akebia, to render all signatures that shall be necessary for such patent filings and to assist Akebia in all other reasonable ways that are necessary for the issuance of the patents involved as well as for the maintenance and prosecution of such patents. Akebia shall be responsible for [***] of the costs incurred with respect to the prosecution and maintenance of such Joint Patents.

(c) Should Akebia decide that it is no longer interested in maintaining or prosecuting a particular Joint Patent in the Territory during the Term, it shall promptly advise Licensee of this decision. Licensee may, upon written notice to Akebia, assume such prosecution and maintenance at its sole expense Akebia shall assign such Joint Patent to Licensee at no cost to Licensee. Following such assignment, such patent or patent application shall no longer be considered a Joint Patent and shall be considered a Licensee Patent.

Section 9.07 Enforcement and Defense

(a) If either Party becomes aware of any Third Party activity in the Territory, including any Development activity (whether or not an exemption from infringement liability for such Development activity is available under applicable law) that infringes (or that is directed to the Development of a product that would infringe) an Akebia Patent, a Joint Patent or a Licensee Patent covering Improvements, then the Party becoming aware of such activity shall give prompt written notice to the other Party regarding such alleged infringement.

(b) As to Akebia Patents and Joint Patents, Akebia shall have the first right, but not the obligation, to attempt to resolve such Third Party activity by commercially appropriate steps at its own expense, including the filing of an infringement suit using counsel of its own choice. If Akebia fails to resolve such Third Party activity or to initiate a suit with respect thereto within [***] days after the notice provided under **Section 9.07** (**Enforcement and Defense**), then, with Akebia's written consent (which shall not be unreasonably withheld, conditioned or delayed), Licensee shall have the right, but not the obligation, to attempt to resolve such Third Party activity by commercially appropriate steps at its own expense, including the filing of an infringement suit using counsel of its own choice. As to Licensee Patents that cover Improvements, Licensee shall have the first right, but not the obligation, to attempt to resolve such Third Party activity by commercially appropriate steps at its own expense, including the filing of an infringement suit using counsel of its own choice. If Licensee fails to resolve such Third Party activity or to initiate a suit with respect thereto within [***] days after the notice provided under **Section 9.07** (**Enforcement and Defense**), then, with Licensee's written consent (which shall not be unreasonably withheld, conditioned or delayed), Akebia shall have the right, but not the obligation, to attempt to resolve such Third Party activity by commercially appropriate steps at its own expense, including the filing of an infringement suit using counsel of its own choice.

(c) Any amounts recovered by a Party as a result of an action pursuant to this **Section 9.07** (**Enforcement and Defense**), whether by settlement or judgment, shall be allocated, after deducting both Parties' internal and external costs associated with the enforcement action, as follows: Licensee shall receive [***] of any amounts recovered and Akebia shall receive [***] of any amounts recovered under this **Section 9.07** (**Enforcement and Defense**).

(d) In any event, at the request and expense of the Party bringing an infringement action under this **Section 9.07** (**Enforcement and Defense**), the other Party shall provide reasonable assistance in any such action (including entering into a common interest agreement if reasonably deemed necessary by any Party) and to be joined as a party to the suit if necessary for the initiating Party to bring or continue an infringement action hereunder. Neither Party may

settle any action or proceeding brought under this **Section 9.07** (**Enforcement and Defense**) in a manner that materially adversely affects the other Party's interest in the Akebia Patents, Joint Patents or Licensee Patents covering Improvements, or knowingly take any other action in the course thereof, without the written consent of such other Party. Each Party shall always have the right to be represented by counsel of its own selection and its own expense in any suit or other action instituted by the other Party pursuant to this **Section 9.07** (**Enforcement and Defense**).

Section 9.08Defense of Third Party Infringement Claims.

(a) If a Third Party asserts that a Patent or other right controlled by it in the Territory is infringed by a Party's activities or a Party becomes aware of a Patent or other right that might form the basis for such a claim, the Party first obtaining knowledge of such a claim or such potential claim shall immediately provide the other Party with notice thereof and the related facts in reasonable detail. The Parties shall discuss whether to take commercially appropriate steps to avoid infringement of said Third Party Patent or other right controlled by such Third Party in the Territory. Akebia will reasonably consider Licensee's comments regarding the avoidance of infringement in the Territory, however, [***].

(b) Notwithstanding the provision set forth in **Section 9.08(a)** that states [***], at any time during the Term, [***] during the exercise of the rights herein granted, whether or not there has been the [***], Licensee may request that [***]. Following such request, Akebia shall [***].

(c) If, during the Term of the Agreement, a Third Party asserts that a Patent or other right controlled by such Third Party is infringed in the Territory by the exercise of the rights herein granted, Akebia will be solely responsible for defending against any such claim at its own expense using Commercially Reasonable Efforts and the counsel of its own choosing. [***].

(d) At any time during the Term, Akebia may at its sole discretion [***]. Akebia shall invoice Licensee for such amounts on a quarterly basis, and such invoices shall be paid by Licensee within [***] days after receipt. This **Section 9.08** (**Defense of Third Party Infringement Claims**) shall not be interpreted as placing on either Party a duty of inquiry regarding Third Party intellectual property rights.

Section 9.09 Patent Term Extensions. Akebia shall be solely responsible for making all decisions regarding patent term extensions, including supplementary protection certificates and any other extensions, that are now available or become available in the future, that are applicable to Akebia Patents and Joint Patents licensed hereunder and that become available directly as a result of the Regulatory Approval of a Licensed Product by Licensee or any of its Affiliates or sublicensees, provided that Akebia shall consult with Licensee with respect to such decisions and shall consider the comments and concerns of Licensee in good faith.

Section 9.10 Trademarks. Licensee shall be responsible for the registration and maintenance of the Licensee Trademarks throughout the Territory, as well as all expenses associated therewith. Akebia shall be responsible for the registration and maintenance of the Akebia Trademarks throughout the Territory, as well as all expenses associated therewith.

ARTICLE X.

INFORMATION AND ADVERSE DRUG EVENTS AND REPORTS

Section 10.01 Information. Akebia and Licensee will use Commercially Reasonable Efforts to disclose and make available to each other in a timely manner all Regulatory Information, Clinical Data, commercial and other information concerning the Licensed Product

or Licensed Compound, known by Akebia or Licensee at any time during the Term of this Agreement (the "**Information**"), subject to receipt of any required Third Party consents. Notwithstanding the foregoing, neither Party shall be obligated to disclose to the other Party confidential information about its products other than the Licensed Product or Licensed Compound.

Section 10.02 Data Security. During the Term of this Agreement, each Party will maintain (and, as applicable, cause its Affiliates to maintain) environmental, safety and facility procedures, data security procedures and other safeguards against the disclosure, destruction, loss, or alteration of the other Party's Information in the possession of such Party or its Affiliates which are no less rigorous than those maintained by such Party (or any of its Affiliates) for its own Information of a similar nature.

Section 10.03 Compliance. Each Party shall maintain a record of all non-medical and medical product-related complaints it receives with respect to any Licensed Product or Licensed Compound. Each Party shall notify the other Party of any such complaint received by it in sufficient detail and in accordance with the timeframes and procedures for reporting established by the Joint Pharmacovigilance Committee ("**JPC**"), and in any event in sufficient time to allow the Party that holds the applicable regulatory filing to comply with any and all regulatory requirements imposed upon it in any country within its territory including in accordance with International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use ("**ICH**") guidelines. The Party that holds the applicable regulatory filing in a particular country shall investigate and respond to all such complaints in such country with respect to any Licensed Product or Licensed Compound as soon as reasonably practicable. All such responses shall be made in accordance with the procedures established by the JPC pursuant to ICH guidelines. The Party responsible for responding to such complaint shall promptly provide the other Party a copy of any such response.

Section 10.04 Adverse Drug Events.

(a) [***] days prior to the commencement of any non-clinical or clinical study in the Territory, the Parties shall enter into a Safety Data Exchange Agreement. Such Safety Data Exchange Agreement shall provide for the exchange by the Parties of any information of which a Party becomes aware in the Territory concerning any adverse event experienced by a subject or, in the case of non-clinical studies, an animal in a toxicology study, and the seriousness thereof, whether or not determined to be attributable to any Licensed Product or Licensed Compound, including any such information received by either Party from a Third Party (subject to receipt of any required consents from such Third Party). It is understood that each Party and its Affiliates or licensees/sublicensees shall have the right to disclose such information if such disclosure is reasonably necessary to comply with applicable laws, regulations, and requirements of Regulatory Authorities within its respective territory with respect to its filings and activities related to the Licensed Compound and Licensed Product. The Safety Data Exchange Agreement will also detail the Parties' responsibilities relating to recalls and withdrawals of a Licensed Product.

(b) The Parties shall, within [***] days after execution of this Agreement, form the JPC which shall include [***] members: [***] designated by Akebia and [***] designated by Licensee. [***] shall be one of the Akebia representatives and serve as chairperson of the JPC. The JPC shall establish a charter that governs the operation of the JPC. For the avoidance of doubt, the JPC shall not be a Sub-Committee of the JSC.

ARTICLE XI.

REPRESENTATIONS, WARRANTIES, AND COVENANTS

Section 11.01 Mutual Representations and Warranties. Each of Licensee and Akebia hereby represents, warrants and covenants (as to (**Section 11.01(h)**):

(a) it is a corporation or entity duly organized and validly existing under the laws of the state, municipality, provinces, administrative division or other jurisdiction of its incorporation or formation;

(b) the execution, delivery and performance of this Agreement by it has been duly authorized by all requisite corporate action;

(c) it has the power and authority to execute and deliver this Agreement and to perform its obligations hereunder, and such performance does not conflict with or constitute a breach of any of its agreements with Third Parties;

(d) it has the right to grant the rights and licenses described in this Agreement, free and clear of all liens, claims or encumbrances;

(e) it has not made any commitments to Third Parties in conflict with the rights granted by it hereunder and it will not do so during the Term of this Agreement;

(f) to its knowledge, no consent, approval or agreement of any person, party, court, government or entity is required to be obtained in connection with the execution and delivery of this Agreement;

(g) it has not been debarred by the FDA, is not the subject of a conviction described in Section 306 of the FD&C Act, an is not subject to any similar sanction of other governmental authorities outside the Territory, and neither it nor any of its Affiliates has used, in any capacity, any person who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any such similar sanction. Neither Party shall engage, in any capacity in connection with this Agreement or any ancillary agreements, any person who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any such similar sanction. Each Party shall inform the other Party in writing promptly if it or any person engaged by Akebia or any of its Affiliates who is performing services under this Agreement, or any ancillary agreements, is debarred or is the subject of a conviction described in Section 306 of the FD&C Act, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to each Party's knowledge, is threatened, relating to the debarment or conviction of a Party, any of its Affiliates or any such person performing services hereunder or thereunder; and

(h) it will comply with all applicable laws and regulations in performing its activities hereunder.

Section 11.02 Additional Akebia Warranties. Akebia hereby represents and warrants as of the Effective Date and covenants (as to **Section 11.02(k)**) that:

(a) to Akebia's knowledge, Exhibit A contains a list of all Akebia Patents that are necessary or useful to make, have made, use, import, offer for sale, and sell the Licensed Compounds and Licensed Products in the Field in the Territory;

(b) to Akebia's knowledge, the Akebia Patents listed in Exhibit A have not expired or been abandoned and Akebia is unaware of any challenge in the Territory to the validity of any of the Akebia Patents listed in Exhibit A;

(c) to Akebia's knowledge, the patent applications included in the Akebia Patents as of the Effective Date have been duly filed in the Territory and the filing, prosecution and maintenance of Akebia Patents and patent applications in the Territory has been conducted in accordance with applicable laws and are pending with the applicable governmental agency, and any and all maintenance fees, annuity fees and renewal fees with respect to any of Akebia Patents that are due and payable have been paid;

(d) to Akebia's knowledge, there is no threatened or pending litigation relating to it or any Affiliate that seeks to invalidate any of the Akebia Patents in the Territory;

(e) to Akebia's knowledge, Akebia has obtained the assignment of all interests and all rights of any and all Third Parties who are entitled to be named as inventors with respect to the subject matter of the Akebia Patents in the Territory;

(f) to Akebia's knowledge, there is no use, infringement or misappropriation of the Akebia Technology in the Territory in derogation of the rights granted to Licensee in this Agreement;

(g) to Akebia's knowledge, there are no investigations, inquiries, actions or other proceedings pending before or threatened by any Regulatory Authority or other government agency in the Territory with respect to the Licensed Product arising from any default by Akebia or a Third Party acting on behalf Akebia in the discovery or Development of the Licensed Compound, and Akebia has not received written notice threatening any such investigation, inquiry, action or other proceeding;

(h) to Akebia's knowledge, Akebia has taken Commercially Reasonable Efforts to protect the secrecy, confidentiality and value of all Know-How that constitutes trade secrets under applicable law (including requiring all employees, consultants and independent contractors to execute binding and enforceable agreements requiring such employees, consultants and independent contractors to maintain the confidentiality of such Know-How) and, to Akebia's knowledge, such Know-How has not been used, disclosed to or discovered by any Third Party except pursuant to such confidentiality agreements and there has not been a breach by any party of such confidentiality agreements;

(i) to Akebia's knowledge, Akebia owns or has licensed the rights, title and interest in and to the Akebia Technology granted to Licensee pursuant to **Section 2.01** (**Grant of License**) of this Agreement;

(j) to Akebia's knowledge, neither the Akebia Technology nor its use infringes any Patent right of any Third Party in the Territory; and

(k) Akebia and its Affiliates shall not (i) license, sell, assign or otherwise transfer to any Third Party any licensed Akebia Technology (or agree to do any of the foregoing) or (ii) incur or permit to exist, with respect to any licensed Akebia Technology, any lien, encumbrance, charge, security interest, mortgage, liability, grant of license to Third Parties or other restriction (including in connection with any indebtedness), *in either case*, that would conflict with the rights granted to Licensee hereunder.

Section 11.03 Additional Licensee Warranties.

(a) Anti-Corruption Provisions. Akebia and Licensee have not, directly or indirectly, offered, promised, paid, authorized or given, and will not in the future, offer, promise, pay, authorize or give, money or anything of value, directly or indirectly, to any Government Official (as defined below) or Other Covered Party (as defined below) for the purpose, pertaining to this

Agreement, of: (i) influencing any act or decision of the Government Official or Other Covered Party; (ii) inducing the Government Official or Other Covered Party to do or omit to do an act in violation of a lawful duty; (iii) securing any improper advantage; or (iv) inducing the Government Official or Other Covered Party to influence the act or decision of a government or government instrumentality, in order to obtain or retain business, or direct business to, any person or entity, in any way related to this Agreement.

For purposes of this Agreement: (i) "**Government Official**" means any official, officer, employee or representative of: (A) any federal, state, provincial, administrative division, county or municipal government or any department or agency thereof; (B) any public international organization or any department or agency thereof; or (C) any company or other entity owned or controlled by any government; and (ii) "**Other Covered Party**" means any political party or party official, or any candidate for political office.

(b) Anti-Corruption Compliance.

(i) In performing under this Agreement, both Parties and their respective Affiliates agree to comply with all applicable anti-corruption laws, including, without limitation: the Foreign Corrupt Practices Act of 1977, as amended from time to time ("**FCPA**"); the anti-corruption laws of the Territory; and all laws enacted to implement the Organization for Economic Co-operation and Development Convention on Combating Bribery of Foreign Officials in International Business Transactions.

(ii) Neither Party is aware of any Government Official or Other Covered Party having any financial interest in the subject matter of this Agreement or in any way personally benefiting, directly or indirectly, from this Agreement.

(iii) No political contributions or charitable donations shall be given, offered, promised or paid at the request of any Government Official or Other Covered Party that is in any way related to this Agreement or any related activity, without the other Party's prior written approval.

(iv) In the event that a Party violates the FCPA, the anti-corruption laws of the Territory or any applicable anti-corruption law or breaches any provision in this Section, the other Party shall have the right to unilaterally terminate this Agreement pursuant to **Section 14.02** (**Termination for Breach**).

Section 11.04 Disclaimer. EXCEPT AS EXPRESSLY SET FORTH HEREIN, THE INTELLECTUAL PROPERTY RIGHTS PROVIDED BY AKEBIA ARE PROVIDED "AS IS" AND WITHOUT WARRANTY. EXCEPT AS EXPRESSLY SET FORTH HEREIN, EACH OF THE PARTIES EXPRESSLY DISCLAIMS ANY AND ALL WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING THE WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY AND/OR ENFORCEABILITY OF THEIR RESPECTIVE INTELLECTUAL PROPERTY RIGHTS, AND NONINFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES, ARISING FROM A COURSE OR DEALING, USAGE OR TRADE PRACTICES, IN ALL CASES WITH RESPECT THERETO.

Section 11.05 Limitation of Liability. NEITHER OF THE PARTIES SHALL BE ENTITLED TO RECOVER FROM THE OTHER PARTY ANY SPECIAL, INCIDENTAL, INDIRECT, CONSEQUENTIAL OR PUNITIVE DAMAGES OR DAMAGES FOR LOSS OF

PROFIT OR LOST OPPORTUNITY IN CONNECTION WITH THIS AGREEMENT, ITS PERFORMANCE OR LACK OF PERFORMANCE HEREUNDER, OR ANY LICENSE GRANTED HEREUNDER. THE FOREGOING SHALL NOT LIMIT ANY INDEMNIFICATION OBLIGATIONS HEREUNDER.

ARTICLE XII.

CONFIDENTIALITY

Section 12.01 Generally. During the Term of this Agreement and for a period of five (5) years following the early termination of this Agreement, each Party (a) shall maintain in confidence all Confidential Information of the other Party; (b) shall not use such Confidential Information for any purpose except in connection with the activities contemplated by this Agreement or in order to further the purpose of this Agreement; and (c) shall not disclose such Confidential Information to anyone other than those of its Affiliates, investors, prospective investors, lenders, prospective lenders, prospective acquirers, permitted sublicensees, prospective sublicensees, employees, consultants, financial or legal advisors, agents or subcontractors who are bound by written obligations of nondisclosure and non-use no less stringent than those set forth in this Article XII **(Confidentiality)** and to whom such disclosure is necessary in connection with such Party's activities as contemplated in this Agreement or in connection with financing or acquisition activities. Each Party shall ensure that such Party's Affiliates, investors, prospective investors, lenders, prospective lenders, acquirors, prospective acquirors, permitted sublicensees, prospective sublicensees, employees, consultants, agents, consultants and subcontractors comply with these obligations. Each Party shall notify the other Party promptly on discovery of any unauthorized use or disclosure of the other's Confidential Information, including the other's trade secrets or proprietary information. Licensee acknowledges that all information related to Akebia's and its Affiliates' and sublicensees' Development and Commercialization of the Licensed Product constitutes Confidential Information of Akebia.

Section 12.02 Exceptions. The obligations of confidentiality, non-disclosure, and non-use set forth in Section 12.01 (Generally) shall not apply to the extent the receiving Party (the "**Recipient**") can demonstrate that the disclosed information (a) was in the public domain at the time of disclosure to the Recipient by the other Party, or thereafter entered the public domain, in each case other than as a result of actions of the Recipient, its Affiliates, employees, licensees, agents or subcontractors, in breach of this Agreement; (b) was rightfully known by the Recipient or its Affiliates (as shown by its written records) prior to the date of disclosure to the Recipient by the other Party; (c) was received by the Recipient or its Affiliates on an unrestricted basis from a Third Party rightfully in possession of such information and not under a duty of confidentiality to the other Party; or (d) was independently developed by or for the Recipient or its Affiliates without reference to or reliance on the Confidential Information of the other Party (as demonstrated by written records). Notwithstanding any other provision of this Agreement, Recipient's disclosure of Confidential Information shall not be prohibited if such disclosure: (i) is in response to a valid order of a court or other governmental body; or (ii) is otherwise required by applicable law or regulation or rules of a nationally recognized securities exchange. Further notwithstanding any other provision of this Agreement, either Party may disclose the other Party's Confidential Information to the extent necessary to exercise the rights granted to or retained by the Recipient under this Agreement, including but not limited in filing or prosecuting patent applications, prosecuting or defending litigation, responding to an investigation by a governmental authority, or otherwise establishing rights or enforcing obligations under this Agreement, making Regulatory Filings with respect to Licensed Product in their respective territories and fields of use, or conducting Development with respect to the Licensed Product. If a Recipient is required to disclose Confidential Information pursuant to this Section 12.02 (**Exceptions**), prior to any disclosure the Recipient shall provide the other

Party with prior written notice of such disclosure in order to permit the other Party to seek a protective order or other confidential treatment of such Confidential Information.

Section 12.03 Publicity. The Parties recognize that each Party may from time to time desire to issue press releases and make other public statements or disclosures regarding the terms of this Agreement. In such event, the Party desiring to issue a press release or make a public statement or disclosure shall provide the other Party with a copy of the proposed press release, statement or disclosure for review and approval as soon as practicable prior to publication, which advance approval shall not be unreasonably withheld, conditioned or delayed. No other public statement or disclosure of, or concerning, the terms of this Agreement shall be made, either directly or indirectly, by either Party hereto, without first obtaining the written approval of the other Party. Once any public statement or disclosure has been approved in accordance with this Section 12.03 (**Publicity**), then either Party may appropriately communicate information contained in such permitted statement or disclosure. Notwithstanding the foregoing provisions of this Article XII (**Confidentiality**), a Party may (a) disclose the terms of this Agreement where required, as reasonably determined by the disclosing Party, by applicable law, regulation or legal process or by applicable stock exchange rule (with prompt notice of any such legally required disclosure to the other Party and to the extent practicable an opportunity to comment on such disclosure) and (b) disclose the terms of this Agreement under obligations of confidentiality to such Party's Affiliates, investors, prospective investors, lenders, prospective lenders, acquirors, prospective acquirors, permitted sublicensees, prospective sublicensees, employees, consultants, agents and subcontractors in connection with such Party's activities hereunder and in connection with such Party's financing activities.

Section 12.04 Publications. The JSC will coordinate the plans of the Parties regarding planned publication in the Territory of Clinical Data or other clinical or preclinical results relating to the Licensed Compound or Licensed Product into a single schedule ("**Joint Publication Plan**") that will be shared with the Parties. With respect to publication in any academic journal, authorship of any publication shall be determined based on the accepted standards used in peer-reviewed, academic journals at the time of the proposed publication. Notwithstanding the forgoing, each Party recognizes the mutual interest in obtaining valid Patent protection and in protecting business interests and trade secret information. Consequently, except for disclosures permitted pursuant to Section 12.02 (**Exceptions**), if either Party, its employees or consultants wishes to publish or present to any Third Party results of the Development work, or any research results, or any Clinical Data or other clinical information about a Licensed Compound, Licensed Product, Bundled Product, or Combination Product being Developed pursuant to this Agreement, it shall deliver to the other Party a copy of the proposed written publication or an outline of an oral disclosure as soon as practicable prior to submission for publication or presentation. The reviewing Party shall notify the other Party promptly after of receipt of such proposed publication whether such draft publication contains (i) Confidential Information of the reviewing Party, or (ii) information that if published would have an adverse effect on a Patent. The reviewing Party shall have the right to (a) propose modifications to the publication or presentation for Patent reasons, trade secret reasons, confidentiality reasons or business reasons and/or (b) request a reasonable delay in publication or presentation in order to protect patentable information. If the reviewing Party requests a delay to protect patentable information, the publishing Party shall delay submission or presentation for a period not to exceed [***] days to enable Patent applications protecting each Party's rights in such information to be filed in accordance with the terms of this Agreement. Upon expiration of such [***] days, the publishing Party shall be free to proceed with the publication or presentation. If the reviewing Party reasonably requests modifications to the publication or presentation to prevent disclosure of material trade secret or proprietary business information, the publishing Party shall edit such publication to prevent the disclosure of such information prior to submission of the publication or presentation.

Section 12.05 Injunctive Relief. Each Party acknowledges and agrees that there may be no adequate remedy at law for any breach of its obligations under this Article XII (**Confidentiality**), that any such breach may result in irreparable harm to such other Party and, therefore, that upon any such breach or any threat thereof, such other Party may seek appropriate equitable relief in addition to whatever remedies it might have at law, without the necessity of showing actual damages.

ARTICLE XIII.

INDEMNIFICATION

Section 13.01 Indemnification by Akebia. Unless otherwise provided herein, Akebia shall indemnify, hold harmless and defend Licensee and its Affiliates, directors, officers, employees and agents (the "**Licensee Indemnitees**") from and against any and all Third Party suits, claims, actions, demands, liabilities, expenses and/or losses (including reasonable attorneys' fees, court costs, witness fees, damages, judgments, fines and amounts paid in settlement) ("**Losses**") to the extent that such Losses arise out of (a) a breach of this Agreement by Akebia, (b) the Development, manufacture, distribution, storage, transportation, use, testing, promotion, marketing, sale or other disposition of a Licensed Product by or on behalf of Akebia or its sublicensees outside the Territory, or the conduct of the Global Phase 3 Program in the Territory or (c) the negligence or willful misconduct of any Akebia Indemnitee (as defined in Section 13.02 (**Indemnification by Licensee**)). Notwithstanding the foregoing, Akebia shall not have any obligation to indemnify the Licensee Indemnitees to the extent that any Losses arise out of the negligence or willful misconduct of any Licensee Indemnitee or any breach of this Agreement by Licensee.

Section 13.02 Indemnification by Licensee. Unless otherwise provided herein, Licensee shall indemnify, hold harmless and defend Akebia and any its Affiliates, directors, officers, employees and agents (the "**Akebia Indemnitees**") from and against any and all Losses, to the extent that such Losses arise out of (a) a breach of this Agreement by Licensee, (b) the Development, manufacture, distribution, storage, transportation, use, testing, promotion, marketing, sale or other disposition of a Licensed Product by or on behalf of Licensee or its sublicensees inside the Territory or (c) the negligence or willful misconduct of any Licensee Indemnitee. Notwithstanding the foregoing, Licensee shall not have any obligation to indemnify the Akebia Indemnitees to the extent that any Losses arise out of the negligence or willful misconduct of any Akebia Indemnitee or any breach of this Agreement by Akebia.

Section 13.03 Procedure. In the event of a claim by a Third Party against a Party entitled to indemnification under this Agreement ("**Indemnified Party**"), the Indemnified Party shall notify the other Party ("**Indemnifying Party**") within five (5) Business Days in writing of the claim and the Indemnifying Party shall undertake and solely manage and control, at its sole expense, the defense of the claim and its settlement. The Indemnified Party shall cooperate with the Indemnifying Party. The Indemnified Party may, at its option and expense, be represented in any such action or proceeding by counsel of its choice. The Indemnifying Party shall not be liable for any litigation costs or expenses incurred by the Indemnified Party without the Indemnifying Party's written consent. The Indemnifying Party shall not settle any such claim unless such settlement fully and unconditionally releases the Indemnified Party from all liability relating thereto, unless the Indemnified Party otherwise agrees in writing.

Section 13.04 Insurance. Each Party shall, at its own expense, obtain and maintain insurance with respect to the Development and Commercialization of Licensed Compounds and Licensed Products under this Agreement in such amount and subject to such deductibles and other limitations as biopharmaceutical companies in the Territory customarily maintain with

respect to the research, development, and commercialization of similar products. Each Party shall provide a copy of such insurance policy to the other Party upon request.

ARTICLE XIV.

TERM AND TERMINATION

Section 14.01 Term. The term of this Agreement shall begin on the Effective Date and, unless earlier terminated in accordance with the terms of this Article XIV (**Term and Termination**), will expire upon the expiration of the Royalty Term (the "**Term**"). Upon the expiration of this Agreement in accordance with the preceding sentence, the licenses granted pursuant to Section 2.01 (**Grant of License**) shall become royalty-free, fully paid up licenses with no additional payments and no royalties due hereunder (other than amounts previously accrued prior to the expiration of the Royalty Term). For clarity, no royalties shall be due under Section 8.04 (**Royalties**) of this Agreement following the expiration of the Royalty Term. Notwithstanding the expiration of the Term, any and all supply agreements entered into by the Parties in accordance with **Section 7.01 (Manufacture and Supply of Licensed Products)** hereof shall continue in accordance with their terms.

Section 14.02 Termination for Breach. Subject to the terms and conditions of this Section 14.02 (**Termination for Breach**), a Party (the "**Non-Breaching Party**") shall have the right, in addition to any other rights and remedies, to terminate this Agreement in the event the other Party (the "**Breaching Party**") is in material breach of its obligations under this Agreement. The Non-Breaching Party shall first provide written notice to the Breaching Party, which notice shall identify with particularity the alleged breach. With respect to material breaches of any payment provision hereunder, the Breaching Party shall have a period of [***] days after such written notice is provided to cure such breach. With respect to all other breaches, the Breaching Party shall have a period of [***] days after such written notice is provided to cure such breach. If such breach is not cured within the applicable period set forth above, the Non-Breaching Party shall have a period of [***] days to (i) enter into good faith discussions with the Breaching Party regarding potential alternatives to termination, and/or (ii) terminate this Agreement upon written notice to the Breaching Party, unless the Breaching Party has commenced a cure and is diligently pursuing such cure at the end of such period, pursuant to an acceptable plan for such cure approved by the other Party, such approval not to be unreasonably withheld, conditioned or delayed. Notwithstanding the foregoing, if a Party gives to the other Party a notice pursuant to this Section 14.02 (**Termination for Breach**) of a material breach by such other Party, and such other Party provides notice during the applicable cure period set forth above that such other Party disputes the basis for termination pursuant to this Section 14.02 (**Termination for Breach**), then this Agreement shall not terminate unless and until an arbitrator issues a final award pursuant to **Section 15.02** (**Arbitration**) upholding such basis for termination provided that the resolution of such dispute is promptly commenced and diligently pursued by the non-terminating Party. The waiver by either Party of any breach of any term or condition of this Agreement shall not be deemed a waiver as to any subsequent or similar breach.

Section 14.03 Termination for Convenience. At any time after the second anniversary of the Effective Date, Licensee shall have the right to terminate this Agreement for convenience upon twelve (12) months prior written notice, which notice period may be shortened by Akebia in its sole discretion.

Section 14.04 Termination for Bankruptcy. To the extent permitted under applicable laws, if at any time during the Term, an Event of Bankruptcy (as defined below) relating to either Party (the "**Bankrupt Party**") occurs, the other Party (the "**Other Party**") shall have, in addition to all other legal and equitable rights and remedies available hereunder, the

option to terminate this Agreement upon sixty (60) days written notice to the Bankrupt Party. It is agreed and understood that if the Other Party does not elect to terminate this Agreement upon the occurrence of an Event of Bankruptcy, except as may otherwise be agreed with the trustee or receiver appointed to manage the affairs of the Bankrupt Party, the Other Party shall continue to make all payments required of it under this Agreement as if the Event of Bankruptcy had not occurred, the Bankrupt Party shall not have the right to terminate any license granted herein. The term "**Event of Bankruptcy**" means: (i) filing in any court or agency pursuant to any statute or regulation of any state or country, a petition in bankruptcy or insolvency or for reorganization or for an arrangement or for the appointment of a receiver or trustee of the Bankrupt Party or of its assets or (ii) being served with an involuntary petition against the Bankrupt Party, filed in any insolvency proceeding, and such petition shall not be dismissed within sixty (60) days after the filing thereof. Without limitation, the Bankrupt Party's rights under this Agreement shall include those rights afforded by 11 U.S.C. § 365(n) of the United States Bankruptcy Code (the "**Bankruptcy Code**") and any successor thereto. If the bankruptcy trustee of a Bankrupt Party as a debtor or debtor-in-possession rejects this Agreement under 11 U.S.C. § 365(o) of the Bankruptcy Code, the Other Party may elect to retain its rights licensed from the Bankrupt Party hereunder (and any other supplementary agreements hereto) for the duration of this Agreement and avail itself of all rights and remedies to the full extent contemplated by this Agreement and 11 U.S.C. § 365(n) of the Bankruptcy Code, and any other relevant laws.

Section 14.05 Effect of Termination by Akebia. In the event of any termination of this Agreement by Akebia pursuant to Section 14.02 (Termination for Breach), the following shall apply:

(a) Licensee shall cease using the Akebia Technology and return all inventory of the Licensed Compound and Licensed Product to Akebia together with all copies of the Akebia Know-How and other Confidential Information in the possession or control of Licensee and its Affiliates and sublicensees;

(b) Akebia shall have, and Licensee hereby grants to Akebia with effect from the date of termination, a non-exclusive, fully paid-up, worldwide right and license, with the right to grant sublicenses in multiple tiers, under all Improvements, Licensee Patents, Licensee Inventions and Licensee Technology originating during the Term to research, develop, make, have made, use, import, offer for sale, sell and otherwise exploit the Licensed Compound in the Field inside and outside the Territory, alone or as incorporated into a Licensed Product, only to the extent necessary or useful to research, develop, make, have made, use, import, offer for sale, sell and otherwise exploit the Licensed Compounds, Licensed Products, Combination Products or Bundled Products in the Field inside and outside the Territory; *provided that* such license shall exclude any Third-Party owned patents, inventions and technology unless Licensee has rights to grant a license to such intellectual property pursuant to the terms of the license from the Third Party. If Licensee is unable to sub-license any patents, inventions or know-how owned by Third Parties to Akebia pursuant to this **Section 14.05(b)** without the consent of the Third Party, Licensee undertakes, on request from Akebia, to use its reasonable endeavors to procure such licenses on behalf of Akebia in as far as they are able to do so and Akebia will pay such fees and agree to be bound by the terms agreed between Akebia and the Third Party licensor;

(c) Licensee shall, at Akebia's written request, promptly (and in any event within [***] days after Licensee's receipt of such request): (1) assign and transfer to Akebia all of Licensee right, title, and interest in and to all Regulatory Filings, Regulatory Approvals, clinical trial agreements (to the extent assignable and not cancelled), confidentiality and other agreements and data relating to Development or Commercialization of Licensed Products, including data, materials, and Know-How relating to clinical trials, in each case to the extent in Licensee's Control and to the extent related to the Licensed Product in the Territory; and

(2) disclose to Akebia all documents, which are in Licensee's Control or which it is able to obtain using reasonable efforts, embodying the foregoing; and

(d) the costs associated with the assignments set forth in **Section 14.05(c)** shall be borne by Licensee.

Section 14.06 Effect of Termination by Licensee. In the event of any termination of this Agreement by Licensee pursuant to Section 14.02 (**Termination for Breach**), the Parties shall enter into good faith discussions regarding a royalty-bearing non-exclusive license from Licensee to Akebia, with the right to grant sublicenses, under all Improvements, Licensee Patents, Licensee Inventions and Licensee Technology to research, develop, make, have made, use, import, offer for sale, sell and otherwise exploit the Licensed Compound in the Field inside and outside the Territory, alone or as incorporated into a Licensed Product, only to the extent necessary or useful to research, develop, make, have made, use, import, offer for sale, sell and otherwise exploit the Licensed Compounds, Licensed Products, Combination Products or Bundled Products in the Field inside and outside the Territory. **Section 14.05(a)** and **Section 14.05(c)** shall apply, and the costs associated with the assignments set forth in **Section 14.05(c)** shall be borne by Akebia. In the event of any termination of this Agreement by Licensee pursuant to Section 14.03 (**Termination for Convenience**), **Section 14.05(a)** through **Section 14.05(d)** shall apply.

Section 14.07 Survival; Accrued Rights. The following articles and sections of this Agreement shall survive expiration or early termination for any reason: Article I (**Definitions**), **Article VIII** (**Payments**) (with respect to any payment obligations incurred prior to expiration or termination), **Section 9**.01 (**Akebia Intellectual Property**), **Section 9.02** (**Licensee Intellectual Property**), **Section 9.03** (**Joint Technology and Improvements**), **Section 9.04** (**Prosecution of Akebia Patents**), **Section 9.05** (**Prosecution of Licensee Patents Covering Improvements**), **Section 9.06** (**Prosecution of Joint Patents**), **Section 9.09** (**Patent Term Extensions**), Article XI (**Representations, Warranties, and Covenants**), Article XII (**Confidentiality**), Article XIII (**Indemnification**), **Section 14.04** (**Termination for Bankruptcy**), Section 14.05 (**Effect of Termination by Akebia**), Section 14.06 (**Effect of Termination by Licensee**), Section 14.07 (**Survival: Accrued Rights**), Article XV (**Dispute Resolution; Governing Law**), and Article XVI (**Miscellaneous**). In any event, expiration or termination of this Agreement shall not relieve the Parties of any liability which accrued hereunder prior to the effective date of such expiration or termination nor preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity with respect to any breach of this Agreement, nor prejudice either Party's right to obtain performance of any obligation.

ARTICLE XV.

DISPUTE RESOLUTION; GOVERNING LAW

Section 15.01 Executive Officers; Disputes. Each Party shall ensure that an executive officer is designated for such Party at all times during the Term of this Agreement for dispute resolution purposes, and shall promptly notify the other Party of any change in its designated executive officer. Unless otherwise set forth in this Agreement, in the event of a dispute arising under this Agreement between the Parties, the Parties shall refer such dispute to the respective executive officers, and such executive officers shall attempt in good faith to resolve such dispute. If the dispute is an Akebia Reserved Dispute, then the executive officer of Akebia shall have the final say on such dispute. If the dispute is a Licensee Reserved Dispute, then the executive officer of Licensee shall have the final say on such dispute.

Section 15.02 Arbitration. If the Parties are unable to resolve a given dispute, other than an Akebia Reserved Dispute or a Licensee Reserved Dispute, [***] days after referring such dispute to the executive officers pursuant to **Section 15.01** (**Executive Officers; Disputes**), then either Party may have the given dispute settled by binding arbitration in the manner described below:

(a) Arbitration Request. If a Party intends to begin an arbitration to resolve a dispute arising under this Agreement, such Party shall provide written notice (the "**Arbitration Request**") to the other Party of such intention and the issues for resolution. From the date of the Arbitration Request and until such time as the dispute has become finally settled, the running of the time periods as to which a Party must cure a breach of this Agreement becomes suspended as to the subject matter of the dispute.

(b) Additional Issues. Within ten (10) days after the receipt of the Arbitration Request, the other Party may, by written notice, add additional issues for resolution.

(c) Arbitration Procedure. Except as expressly provided herein, any dispute, controversy or claim arising out of or in connection with this Agreement, including any question regarding its existence, validity or termination, shall be referred to and finally resolved by arbitration under the London Court of International Arbitration Rules, which rules are deemed to be incorporated by reference into this **Section 15.02(c)** (**Arbitration**). There shall be one arbitrator, and such arbitrator will be chosen pursuant to the London Court of International Arbitration Rules. The seat, or legal place, of arbitration shall be London, England, or such other venue as the Parties agree. The language to be used in the arbitral proceedings shall be English. Nothing in this Agreement shall be deemed as preventing either Party from seeking injunctive relief (or any other provisional remedy) from any court having jurisdiction over the Parties and the subject matter of the dispute as necessary to protect either Party's name, proprietary information, trade secrets, know-how or any other proprietary right or otherwise to avoid irreparable harm. If the issues in dispute involve scientific or technical matters, any arbitrator chosen hereunder shall have educational training and/or experience sufficient to demonstrate a reasonable level of knowledge in the field of biotechnology and pharmaceuticals. Judgment on the award rendered by the arbitrator may be entered in any court having jurisdiction thereof.

Section 15.03 Choice of Law. This Agreement and all amendments, modifications, alterations, or supplements hereto, and the rights of the Parties hereunder, shall be construed under and governed by the laws of the State of New York, United States, exclusive of its conflicts of laws principles. This Agreement has been prepared in the English language and the English language shall control its interpretation. All consents, notices, reports and other written documents to be delivered or provided by a Party under this Agreement shall be in the English language, and in the event of any conflict between the provisions of any document and the English language translation thereof, the terms of the English language translation shall control.

ARTICLE XVI.

MISCELLANEOUS

Section 16.01 Assignment. Either Party may assign this Agreement and the licenses herein granted (a) to any Affiliate of such Party without the prior written consent of the other Party, provided that such Party remains fully liable for the performance of such Party's obligations hereunder by such Affiliate and such Party so informs the other Party of the assignment, (b) prior to [***], with the other Party's prior written consent, (c) [***], with the other Party's prior written consent unless such assignment is to any Third Party purchaser of all or substantially all of the assets or businesses to which this Agreement relates, in which case the

assigning Party will provide prior written notice to the other Party and need not obtain the other Party's consent. Any other assignment of this Agreement by a Party requires the prior written consent of the other Party. Any assignment in violation of this Section 16.01 (**Assignment**) shall be null and void. This Agreement shall be binding on and shall inure to the benefit of the permitted successors and assigns of the Parties hereto.

Section 16.02 Standstill. During the Term, Licensee shall not directly or indirectly, without the prior approval of the Board of Directors of Akebia, acquire common shares of Akebia in the public market or from other shareholders exceeding an aggregate total equity stake of [***] on a fully diluted as converted basis.

Section 16.03 Non-Competition. During the Term of this Agreement, Licensee shall not [***] ("**Competing Product**"). Competing Product shall not include (i) any product set forth in Exhibit B, the contents of which shall be agreed upon by the Parties within thirty (30) days after the Effective Date, or (ii) any product containing [***]. For the avoidance of doubt, this **Section 16.03** (**Non-Competition**) shall not apply to Affiliates of Licensee [***]. Notwithstanding the foregoing, at any time during the Term, if Licensee wishes to promote or sell a Competing Product, Licensee may request Akebia's consent to promote or sell said Competing Product. Following the request by Licensee, the Parties shall enter into good faith discussions regarding such request.

Section 16.04 Additional Collaboration. Within [***] after the Effective Date, the Parties will discuss the [***].

Section 16.05 Force Majeure. If either Party shall be delayed, interrupted in or prevented from the performance of any obligation hereunder by reason of force majeure including an act of God, fire, flood, earthquake, war (declared or undeclared), public disaster, act of terrorism, strike or labor differences, such Party shall not be liable to the other therefor; and the time for performance of such obligation shall be extended for a period equal to the duration of the force majeure which occasioned the delay, interruption or prevention. The Party invoking such force majeure rights of this Section 16.05 (**Force Majeure**) must notify the other Party by courier or overnight dispatch (e.g., Federal Express) within a period of thirty (30) days of both the first and last day of the force majeure unless the force majeure renders such notification impossible in which case notification will be made as soon as possible. If the delay resulting from the force majeure exceeds [***].

Section 16.06 Entire Agreement. This Agreement, together with Exhibit A and Exhibit B attached hereto, constitutes the entire agreement between the Parties with respect to the subject matter hereof and shall not be modified, amended or terminated, except as herein provided or except by another agreement in writing executed by the Parties hereto.

Section 16.07 Severability. If any provision of this Agreement is declared invalid by a court of last resort or by any court or other governmental body from the decision of which an appeal is not taken within the time provided by law, then and in such event, this Agreement will be deemed to have been terminated only as to the portion thereof that relates to the provision invalidated by that decision and only in the relevant jurisdiction, but this Agreement, in all other respects and all other jurisdictions, will remain in force; *provided*, *however*, that if the provision so invalidated is essential to the Agreement as a whole, then the Parties shall negotiate in good faith to amend the terms hereof as nearly as practical to carry out the original intent of the Parties, and, failing such amendment, either Party may submit the matter for resolution pursuant to Article XV (**Dispute Resolution; Governing Law**).

Section 16.08 Notices. Any notice or report required or permitted to be given under this Agreement shall be in writing and shall be mailed by internationally recognized express delivery service, or sent by facsimile and confirmed by mailing, as follows:

If to Akebia:

Akebia Therapeutics, Inc.
245 First Street, Suite 1100
Cambridge, MA 02142, U.S.A.
Attention: Chief Executive Officer
Facsimile:

With a copy to (which shall not constitute notice for purposes of this Agreement):

Akebia Therapeutics, Inc.
245 First Street, Suite 1100
Cambridge, MA 02142
Attention: General Counsel
Facsimile:

If to Licensee:

Mitsubishi Tanabe Pharma Corporation
17-10, Nihonbashi-Koamicho,
Chuo-ku, Tokyo 103-8405, Japan
Attention: General Manager

Business Development Department

Facsimile:

With a copy to (which shall not constitute notice for purposes of this Agreement):

Mitsubishi Tanabe Pharma Corporation
3-2-10 Dosho-machi
Cho-ku, Osaka, Japan
Attention: General Manager

Legal Affairs & Intellectual Property Department

Facsimile:

Section 16.09 Further Assurances. The Parties agree to reasonably cooperate with each other in connection with any actions required to be taken as part of their respective obligations under this Agreement, and shall (a) furnish to each other such further information; (b) execute and deliver to each other such other documents; and (c) do such other acts and things (including working collaboratively to correct any clerical, typographical, or other similar errors in this Agreement), all as the other Party may reasonably request for the purpose of carrying out the intent of this Agreement.

Section 16.10 Agency. Neither Party is, nor will be deemed to be an employee, agent or representative of the other Party for any purpose. Each Party is an independent contractor, not

an employee or partner of the other Party. Neither Party shall have the authority to speak for, represent or obligate the other Party in any way without prior written authority from the other Party.

Section 16.11 No Waiver. Any omission or delay by either Party at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants or provisions hereof, by the other Party, shall not constitute a waiver of such Party's rights to the future enforcement of its rights under this Agreement. Any waiver by a Party of a particular breach or default by the other Party shall not operate or be construed as a waiver of any subsequent breach or default by the other Party.

Section 16.12 No Strict Construction. This Agreement has been prepared jointly by the Parties and shall not be strictly construed against either Party.

Section 16.13 Cumulative Remedies. No remedy referred to in this Agreement is intended to be exclusive, but each shall be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law.

Section 16.14 Counterparts. This Agreement may be executed in counterparts, all of which taken together shall be regarded as one and the same instrument.

IN WITNESS WHEREOF, the Parties have executed this Agreement through their duly authorized representatives to be effective as of the Effective Date.

AKEBIA THERAPEUTICS, INC.

By:	/s/ John P. Butler	By:	/s/ Jason A. Amello
Name:	John P. Butler	Name:	Jason A. Amello
Title:	President & Chief Executive Officer	Title:	Senior Vice President, Chief Financial Officer & Treasurer

MITSUBISHI TANABE PHARMA CORPORATION

By:	/s/ Masayuki Mitsuka
Name:	Masayuki Mitsuka
Title:	President & Representative Director Chief Executive Officer

Exhibit 10.54

CONFIDENTIAL

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omission.

SECOND AMENDED AND RESTATED LICENSE AGREEMENT

BY AND BETWEEN

AKEBIA THERAPEUTICS, INC.

AND

VIFOR (INTERNATIONAL) LTD.

Dated February 18, 2022

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SECOND AMENDED AND RESTATED LICENSE AGREEMENT

THIS SECOND AMENDED AND RESTATED **LICENSE AGREEMENT** (this "**Second Amended Agreement**") is made and entered into as of February 18, 2022 (the "**Effective Date**") between Akebia Therapeutics, Inc., a company organized and existing under the laws of the State of Delaware, United States of America with its principal offices at 245 First Street, Cambridge, MA 02142 ("**Akebia**"), and Vifor (International) Ltd., a corporation established in accordance with Swiss laws and registered in the commercial registry under CH-107.360.718, with its premises at Rechenstrasse 37, 9014 St. Gallen, Switzerland ("**Licensee**").

Akebia and Licensee may be referred to herein individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, Akebia is the owner of, or otherwise controls, the Akebia Technology, the Licensed Compound, and the Licensed Products in the Territory;

WHEREAS, as of the Effective Date, the Licensed Product is an investigational agent that has completed Phase 3 clinical trials for the treatment of anemia secondary to chronic kidney disease for which the safety and effectiveness in the Territory has not yet been established, and, as of such date, an NDA has been filed but the Licensed Product has not yet received Regulatory Approval;

WHEREAS, Licensee has commercial capabilities in the Territory, and is interested in obtaining an exclusive license to sell Licensed Products in the Field in the Territory;

WHEREAS, as of the Effective Date, Vifor Pharma Participations Ltd., the parent company of Licensee, and Fresenius Medical Care AG & Co KGaA ("**FMC**"), the parent company of FMCNA, are joint venture partners of Vifor Fresenius Medical Care Renal Pharma Ltd. ("**VFMCRP**"), with Vifor Pharma Participations Ltd. owning a controlling interest of VFMCRP;

WHEREAS, Licensee and its Affiliates (including VFMCRP) are strategic partners of Fresenius Kidney Care Group LLC, a Delaware limited liability company ("**FKC**") and FreseniusRx, Inc., ("**FreseniusRx**"), each of which is an Affiliate of FMCNA;

WHEREAS, Licensee, indirectly through VFMCRP, has entered into a supply agreement with FKC and intends to enter into supply agreements with one or more approved Specialty Pharmacies (which provide specialty pharmacy services to patients receiving treatment in the DD-CKD Indication), certain approved Third Party Dialysis Organizations, and certain Designated Wholesalers;

WHEREAS, Licensee, directly or indirectly through VFMCRP, intends to enter into supplier agreements with one or more GPOs and IDO Participation Letters with certain approved Independent Dialysis Organization members of such GPOs, and pursuant to such supplier agreements and IDO Participation Letters, Licensed Products will be supplied to such approved Independent Dialysis Organizations;

WHEREAS, pursuant to such supply agreement with FKC, FKC will provide such Licensed Products only to Authorized Dialysis Centers (other than TPDO Clinics and IDO Clinics); pursuant to such supply agreement with Specialty Pharmacies, Licensed Products will be supplied to such Specialty Pharmacies; pursuant to such supply agreements with Third Party Dialysis Organizations, such Third Party Dialysis Organizations will provide such Licensed Products only to TPDO Clinics; and pursuant to such IDO Participation Letters, Independent Dialysis Organizations will provide such Licensed Products only to IDO Clinics;

WHEREAS, Akebia and Licensee are parties to that certain License Agreement dated May 12, 2017 (the "**Original Execution Date**", and such agreement, the "**Original Agreement**") pursuant to which Akebia granted Licensee an exclusive license to sell Licensed Products to FKC in the Field in the

Territory, and to that certain Amended and Restated License Agreement dated April 8, 2019 (the "**First Amended Agreement**") pursuant to which Akebia granted Licensee certain additional rights, including with respect to sales of Licensed Products to Third Party Dialysis Organizations in the Field in the Territory;

WHEREAS, Akebia and Licensee now desire to amend and restate the First Amended Agreement by entering into this Second Amended Agreement (the First Amended Agreement, as amended by this Second Amended Agreement, the "**Agreement**");

WHEREAS, Licensee acknowledges that Akebia has entered into as of the Effective Date, and may during the Term enter into, other agreements with Third Parties with respect to the Licensed Products in the Territory, including granting such Third Parties rights and licenses to Promote or otherwise commercialize such Licensed Products in the Territory, and Licensee agrees that this Agreement is subject to and will be consistent with such agreements; and

WHEREAS, simultaneously with the execution of this Agreement the Parties are entering into the Stock Purchase Agreement (as defined below) pursuant to which Licensee is making an equity investment in Akebia and a Supply Agreement pursuant to which Akebia will supply Licensed Products to Licensee.

NOW THEREFORE, the Parties agree to amend and restate the Agreement to read in its entirety as follows:

Article 1

DEFINITIONS

1.1 **"340B Ceiling Price"** means the price calculated pursuant to Section 340B(a) of the Public Health Service Act, 42 U.S.C. § 256b(a).

1.2 "**Accounting Standards**" means (a) International Financial Reporting Standards, as adopted in Switzerland, (b) U.S. GAAP, or (c) the applicable accounting standards to which the entity making the Net Sales is subject.

1.3 "**Additional Working Capital Payment**" has the meaning set forth in Section 11.5 (Working Capital Fund).

1.4 "**Affiliate**" means, with respect to an entity, any corporation, or other business entity controlled by, controlling, or under common control with the first entity, with "control" meaning direct or indirect beneficial ownership of at least 50% of the voting stock of, or at least a 50% interest in the income of, the applicable entity. For clarity, as of the Effective Date, Licensee is not an Affiliate of FMC, FMCNA or any member of the Licensee Supply Group.

1.5 "**Agreement**" has the meaning set forth in the Recitals.

1.6 "**Akebia**" has the meaning set forth in the Preamble.

1.7 "**Akebia Indemnitees**" has the meaning set forth in Section 15.2 (Indemnification by Licensee).

1.8 "**Akebia Know-How**" means all Know-How that is both (a) Controlled as of the Original Execution Date or during the Term by Akebia or any of its Affiliates, and (b) is either (i) disclosed to Licensee or any of its Affiliates pursuant to this Agreement, or (ii) reasonably necessary for the sale of a Licensed Product.

1.9 "**Akebia Patents**" means all Patents that both (a) are Controlled as of the Effective Date or during the Term by Akebia or any of its Affiliates in the Territory; and (b) [**]. All Akebia Patents as of the Effective Date are set forth on Schedule 1.9.

1.10 "**Akebia Technology**" means Akebia Know-How and Akebia Patents.

1.11 "**Akebia Trademarks**" means one or more trademarks selected by Akebia or its Affiliates or licensees under which Akebia or its Affiliates or licensees [**], as well as the Akebia company name and logo, and all trademark registrations and applications therefor, and all goodwill associated therewith. All Akebia Trademarks as of the Effective Date are set forth on Schedule 1.11.

1.12 "**AMP**" or "**average manufacturer price**" has the meaning set forth in 42 U.S.C. § 1396r-8(k)(1).

1.13 "**API**" means active pharmaceutical ingredient, which is also commonly referred to as drug substance. For the avoidance of doubt, API will include any prodrug form.

1.14 "**Applicable Law**" means any applicable law (including common law), statute, rule, regulation, order, judgment, or ordinance of any Governmental Authority (including the FDA), including those concerning environmental, health, regulatory, privacy, and safety matters.

1.15 **"ASP" or "average sales price"** has the meaning set forth at 42 U.S.C. § 1395w-3a(c) and implementing regulations.

1.16 "**Authorized Dialysis Center**" means (a) the Majority Owned Clinics, FKC Clinics, TPDO Clinics, and IDO Clinics identified on Schedule 5.10 (as the same may be updated from time to time in accordance with Section 5.10 (Licensee Supply Group)), and (b) home dialysis programs administered through the clinics identified in the foregoing clause (a). Notwithstanding anything to the contrary set forth in this Agreement, in no event will "Authorized Dialysis Centers" include dialysis clinics owned, operated or affiliated with [**].

1.17 **"Best Price"** has the meaning set forth in 42 U.S.C. § 1396r-8(c)(1)(C) and implementing regulations.

1.18 "**Breaching Party**" has the meaning set forth in Section 16.2 (Termination for Breach).

1.19 "**Business Day**" means any day (other than a Saturday or Sunday) on which the banks in both Cambridge, Massachusetts and Zurich, Switzerland are open for business.

1.20 "**Clinical Trial**" means any study in humans conducted to obtain information regarding a pharmaceutical or biologic product, including information relating to the safety, tolerability, pharmacological activity, pharmacokinetics, dose ranging, or efficacy of such pharmaceutical or biologic product.

1.21 "**CMS**" means the Centers for Medicare & Medicaid Services.

1.22 "**Combination Product**" means any product that is comprised of two or more APIs, at least one of which is the Licensed Compound, for use in the DD-CKD Indication.

1.23 "**Commercially Reasonable Efforts**" means, with respect to the efforts to be expended by a Party with respect to any objective under this Agreement, those efforts and resources that a company within the biopharmaceutical industry of comparable size and resources would typically devote to accomplishing such similar objective under similar circumstances, in each case, with respect to Akebia's efforts, taking into account the Relevant Factors in effect at the time such efforts are expended.

1.24 "**Competing Product**" means any product or product candidate that is not a Licensed Product and that (a) [**] and is approved for the DD-CKD Indication or the NDD-CKD Indication, or (b) is based on [**]. For the avoidance of doubt, the Parties acknowledge and agree that [**].

1.25 "**Complete Response Letter**" means a complete response letter issued by the FDA in accordance with 21 C.F.R. §314.110.

1.26 "**Confidential Information**" means Know-How and any technical, scientific, trade, research, manufacturing, business, financial, marketing, product, supplier, intellectual property, and other information that may be disclosed by one Party to the other Party pursuant to this Agreement (including information disclosed prior to the Original Execution Date pursuant to a Confidential Disclosure Agreement between the Parties dated [**], as amended by Amendment No. 1 dated [**]), regardless of whether such information is specifically designated as confidential and regardless of whether such information is in written, oral, electronic, or other form.

1.27 "**Controlled**" means, with respect to a Party or its Affiliate, any Know-How, Patents, or other intellectual property right that such Party or Affiliate, as the case may be, owns or has a license to and has the ability to grant to the other Party a license or sublicense to, or a right of access with respect to, such Know-How, Patent, or other intellectual property right without violating the terms of any agreement or other arrangements with any Third Party or incurring any additional payment obligations to a Third Party.

1.28 "**Coordination Committee**" has the meaning set forth in Section 2.1 (Formation and Purpose of the Coordination Committee).

1.29 "**Co-Packaged Product**" means a product that contains a Licensed Product and one or more Other Components and that is either (a) packaged together for sale or shipment as a single unit or sold at a single price, or (b) marketed or sold collectively as a single product.

1.30 "**Cost of Goods Sold**" or "**COGS**" means, with respect to any Licensed Product in [**] (a) for products and services acquired from or performed by Third Parties, the [**] actual amounts [**] such Third Parties to the extent [**]; and (b) to the extent manufacturing services are performed by [**] or its Affiliates, the fully-burdened cost of all direct materials and labor and fully allocated manufacturing overhead directly attributable to the manufacture, storage, packaging, and shipping of a Licensed Product [**], calculated in accordance with the Accounting Standards *provided that* for any Licensed Product manufactured by Akebia, [**] will be excluded from the calculation of COGS. In each case ((a) or (b)), COGS includes all [**], Licensed Product testing and yield loss costs, quality control, quality assurance, or other testing of Licensed Products, together with all reasonably allocated indirect costs and overhead applicable to the manufacturing of each Licensed Product, quality control, or technical operations functions, less costs of resalable goods returned in accordance with Akebia's, or its suppliers', return policy.

1.31 "**Cover**" means with respect to a particular subject matter at issue and a relevant Patent, that the manufacture, use, sale, offer for sale, or importation of the subject matter would fall within the scope of a claim in such Patent.

1.32 "**DD-CKD Indication**" means the treatment of anemia in dialysis patients with chronic kidney disease.

1.33 "**Designated Wholesalers**" means [**].

1.34 "**Dollars**" or "**$**" means the legal tender of the U.S.

1.35 "**Effective Date**" has the meaning set forth in the Preamble.

1.36 "**Effective Period**" has the meaning set forth in Section 3.2.2 (Suspension).

1.37 "**ESA**" means erythropoiesis stimulating agent.

1.38 "**ESRD**" means end-stage renal disease.

1.39 "**ESRD PPS Bundled Payment System**" means Medicare's ESRD prospective payment system for a single per-treatment bundled payment that is made for the collection of renal dialysis products and services furnished to individuals for the treatment of ESRD in an ESRD facility or in a patient's home, as set forth under 42 U.S.C. § 1395rr, as in effect as of the Effective Date.

1.40 "**FDA**" means the U.S. Food and Drug Administration or any successor agency thereto.

1.41 "**Field**" means the treatment of anemia in dialysis patients with chronic kidney disease who receive dialysis either at an Authorized Dialysis Center or through a home dialysis program administered by an Authorized Dialysis Center, in each case, with Licensed Product that has received Regulatory Approval in the DD-CKD Indication and that is provided to such dialysis patients either directly by the Authorized Dialysis Center or through a Specialty Pharmacy.

1.42 "**Finished Form**" means a Licensed Product containing the Licensed Compound as its sole API in the [**] form in any dosage strength that receives Regulatory Approval in the Territory in the DD-CKD Indication, with all applicable packaging and labeling.

1.43 "**First Amended Agreement**" has the meaning set forth in the Recitals.

1.44 "**First Commercial Sale**" means, for each Licensed Product in the Territory, the first sale for end use or consumption to a Third Party of such Licensed Product in the Territory by Licensee or its Affiliates after the granting of Regulatory Approval in the DD-CKD Indication in the Territory for such Licensed Product by the FDA.

1.45 "**FKC**" has the meaning set forth in the Recitals.

1.46 "**FKC Clinics**" means: (a) all dialysis clinics (including home dialysis programs) in the Territory that purchase pharmaceutical products under FMCNA's or FMCNA's Affiliates' formulary guidelines and (b) all dialysis clinics (including home dialysis programs) in the Territory for which FMCNA or its Affiliates provide management or administrative services that include the purchase of pharmaceutical products, but in each case ((a) and (b)) excluding TPDO Clinics and IDO Clinics.

1.47 "**FMC**" has the meaning set forth in the Recitals.

1.47.1 **"FMC Contracting Party"** has the meaning set forth in Section 5.1.2.

1.48 "**FMCNA**" or "**Fresenius Medical Care North America**" means Fresenius Medical Care Holdings, Inc., and any successor entity of all or substantially all of Fresenius Medical Care Holdings, Inc.'s dialysis clinic business in the Territory (by operation of law or by sale, merger, restructuring, or other transfer of direct or indirect ownership of dialysis clinics).

1.49 "**FreseniusRx**" has the meaning given to it in the Recitals.

1.50 "**Governmental Authority**" means any court, agency, department, authority, or other instrumentality of any national, state, county, city, or other political subdivision.

1.51 "**Group Purchasing Organization**" or "**GPO**" means a Third Party organization that (a) manages contracts with its participating members in order to provide pharmaceutical drug purchasing services to its participating members, (b) has entered into a Licensee-GPO Supplier Agreement meeting the requirements set forth in Section 5.6 (Licensee-GPO Supplier Agreement), and (c) has been approved by Akebia and listed on Schedule 5.10 under the heading "Group Purchasing Organizations" (as the same may be updated from time to time in accordance with Section 5.10 (Licensee Supply Group)).

1.52 "**HCPCS Code**" means CMS's Healthcare Common Procedure Coding System.

1.53 "**HIF**" means hypoxia-inducible factor.

1.54 "**Indemnified Party**" has the meaning set forth in Section 15.3 (Indemnification Procedure).

1.55 "**Indemnifying Party**" has the meaning set forth in Section 15.3 (Indemnification Procedure).

1.56 "**IDO Clinics**" means the dialysis clinics (including home dialysis programs) owned by IDOs in the Territory that are identified on Schedule 5.10 under the heading "IDO Clinics" (as the same may be updated from time to time in accordance with Section 5.10 (Licensee Supply Group))

1.57 "**IDO Participation Letter**" means a letter agreement between Licensee and an IDO described in Section 5.7 (IDO Participation Letter).

1.58 "**Independent Dialysis Organization**" or "**IDO**" means an independent Third Party operator of dialysis clinics in the Territory identified on Schedule 5.10 under the heading "Independent Dialysis Organizations" (as the same may be updated from time to time in accordance with Section 5.10 (Licensee Supply Group)) that owns at least one IDO Clinic and (a) is a participating member of a GPO and (b) has executed an IDO Participation Letter in accordance with the requirements of Section 5.7 (IDO Participation Letter).

1.59 "**Initial Working Capital Payment**" has the meaning set forth in Section 11.5 (Working Capital Fund).

1.60 "**Know-How**" means inventions, discoveries, trade secrets, information, experience, data, formulas, procedures, technology and results (whether or not patentable), including practices, knowledge, know-how, experience and test data (including physical, chemical, biological, toxicological, pharmacological, clinical and veterinary data), dosage regimens, control assays, product specifications, analytical and quality control data, marketing, pricing, distribution cost and sales data or descriptions.

1.61 "**Knowledge**" means the actual knowledge of each Party's [**], in each case, without any inquiry or investigation.

1.62 "**License**" has the meaning set forth in Section 3.1 (Grant of License to Licensee).

1.63 "**Licensed Compound**" means vadadustat, and any salt or crystal form thereof. Licensed Compound includes any prodrug form of vadadustat.

1.64 "**Licensed Product**" means any pharmaceutical product, drug product, preparation, formulation, or dosage form thereof that has the Licensed Compound as its API.

1.65 "**Licensed Product Plan**" has the meaning set forth in Section 4.7 (Licensed Product Plan).

1.66 "**Licensee**" has the meaning set forth in the Preamble.

1.67 "**Licensee Compliance Program**" has the meaning set forth in Section 4.10.1 (Compliance).

1.68 "**Licensee Indemnitees**" has the meaning set forth in Section 15.1 (Indemnification by Akebia).

1.69 "**Licensee Supply Group**" means FMCNA, FMCNA's Affiliates (including FKC), Third Party Dialysis Organizations, IDOs, Authorized Dialysis Centers, and Specialty Pharmacies.

1.70 "**Licensee-Designated Wholesaler Supply Agreement**" has the meaning set forth in Section 5.8 (Terms of the Licensee-Designated Wholesaler Supply Agreements).

1.71 "**Licensee-FKC Supply Agreement**" has the meaning set forth in Section 5.1 (Licensee-FKC Supply Agreement).

1.72 "**Licensee-FreseniusRx Supply Agreement**" has the meaning set forth in Section 5.3 (Licensee-FreseniusRx Supply Agreement).

1.73 "**Licensee-GPO Supplier Agreement**" has the meaning set forth in Section 5.6 (Licensee-GPO Supplier Agreement).

1.74 "**Licensee-Specialty Pharmacy Supply Agreement**" has the meaning set forth in Section 5.4 (Terms of the Licensee-Specialty Pharmacy Supply Agreements).

1.75 "**Licensee-TPDO Purchase Agreement**" has the meaning set forth in Section 5.3 (Licensee-TPDO Purchase Agreements).

1.76 "**Licensee's Pre-Termination Sales Volume**" has the meaning set forth in Section 16.10.1 (Termination Fee).

1.77 "**Licensee's Tail Period Profit Share**" has the meaning set forth in Section 16.10.1 (Termination Fee).

1.78 "**Losses**" has the meaning set forth in Section 15.1 (Indemnification by Akebia).

1.79 "**LSP**" has the meaning set forth in Section 5.2.1 (Terms of the Licensee-FKC Supply Agreement).

1.80 "**Majority Owned Clinics**" means all dialysis clinics in the Territory that are Affiliates of FMCNA.

1.81 "**Medical Affairs**" means any and all activities appropriately conducted by or on behalf of a Party's or any of its Affiliates' medical affairs function including: (i) interacting with physicians or other healthcare professionals who utilize or conduct research related to a drug or biological product, including communications with key opinion leaders, medical education, symposia, advisory boards (to the extent related to medical affairs or clinical guidance), and other medical programs and communications, (ii) activities supporting educational grants and fellowships, research grants, investigator-initiated studies, charitable donations, medical and scientific platform, content development, publications, and communications, KME and KOL engagement, and congress planning, (iii) conducting advisory board meetings or other consultant programs, the purpose of which is to obtain advice and feedback related to the launch of a given product, (iv) activities related to patient registries, (v) physician and nurse education, in each case, to the extent related to medical affairs and not to activities that involve the Promotion, marketing, sale, or other commercialization of Licensed Products.

1.82 "**Medical Affairs Committee**" has the meaning set forth in Section 2.4.2 (Medical Affairs Committee).

1.83 "**NDA**" means a New Drug Application or its equivalent for submission to the FDA.

1.84 "**NDD-CKD Indication**" means the treatment of anemia in non-dialysis patients with chronic kidney disease.

1.85 "**Net Sales**" means the gross amounts invoiced by Licensee or its Affiliates for the sales of a Licensed Product in the Territory, to the extent recognized and allowed in accordance with the Accounting Standards, as applicable and consistently applied, less the following deductions:

1.85.1 inventory management fees paid to distributors and reasonably allocated to such Licensed Product, not to exceed [**]% of aggregate Net Sales in the applicable period;

1.85.2 tariffs, duties, excises, value added tax, and other sales taxes, and other taxes imposed upon and paid with respect to the sale, transportation, delivery, use, exportation, or importation of such Licensed Product (which taxes do not include income taxes);

1.85.3 amounts actually repaid or credited upon returns, rejections, defects, recalls (due to spoilage, damage, or expiration of useful life), price adjustments, billing errors, or trial prescriptions;

1.85.4 freight, shipping, and insurance expenses specific to such Licensed Product and allocated accordingly;

1.85.5 allowances or credits actually paid or given to customers on account of price reductions affecting such Licensed Product;

1.85.6 rebates and similar payments made with respect to sales paid for by any governmental or regulatory authority, including interest or penalties thereon, to the extent such rebates or other payments are paid by Akebia and actually reimbursed in full by Licensee to Akebia in accordance with Section 4.5 (Rebates);

1.85.7 discounts actually paid by Licensee or its Affiliates with respect to sales made by Licensee or its Affiliates to FKC, Specialty Pharmacies, TPDOs, and IDOs under state-legislated or Licensee-sponsored discount prescription drug programs or reductions or coupon and voucher programs;

1.85.8 wholesaler service fees and chargebacks actually paid or credited by Licensee or its Affiliates;

1.85.9 discounts actually paid or credited by Licensee or its Affiliates for prompt payment; and

1.85.10 Specialty Pharmacy fees.

Net Sales will be determined from books and records of Licensee or its applicable Affiliate, maintained in accordance with the Accounting Standards, as consistently applied, with respect to sales of any Licensed Product.

The sale of Licensed Products among Licensee or Licensee's Affiliates that are [**], but in such cases Net Sales will [**] of such Licensed Products to a person or entity who is not an Affiliate.

Net Sales will not include Licensed Products transferred for use in connection with promotional use (including samples).

If Licensee or any of its Affiliates receives [**] for a Licensed Product, then the Net Sales amount for such Licensed Product will be [**].

In the event that a Licensed Product is sold as part of a Co-Packaged Product, the Net Sales from the Co-Packaged Product, for the purposes of determining payments hereunder based on Net Sales, will be determined by multiplying the Net Sales of the Co-Packaged Product (as applicable), during the applicable reporting period, by the fraction, A/(A+B), where A is the average sale price of a Licensed Product when sold separately in Finished Form and B is the average sale price of the Other Components included in the Co-Packaged Product when sold separately during the applicable reporting period or, if sales of both such Licensed Product and the Other Components did not occur in such period, then in the most recent reporting period in which sales of both occurred. In the event that such average sale price cannot be determined for both a Licensed Product and all Other Components included in such Co-Packaged Product, then Net Sales for the purposes of determining payments to Akebia hereunder will be

calculated by multiplying the Net Sales of the Co-Packaged Product during the applicable reporting period by the fraction of C/(C+D) where C is the fair market value of a Licensed Product and D is the average sales price of the Other Components included in such Co-Packaged Product when sold separately. In such event, Licensee will in good faith make a determination of the respective fair market values of such Licensed Product and all Other Components included in the Co-Packaged Product.

If a Licensed Product is sold as part of a Co-Packaged Product, then Licensee or its applicable Affiliate [**].

1.86 "**NFAMP**" or "**non-Federal average manufacturer price**" has the meaning set forth in 38 U.S.C. § 8126(h)(5).

1.87 "**Non-Breaching Party**" has the meaning set forth in Section 16.2 (Termination for Breach).

1.88 "**Operational Plan**" has the meaning set forth in Section 4.8 (Operational Plan).

1.89 "**Original Agreement**" has the meaning set forth in the Recitals.

1.90 "**Original Execution Date**" has the meaning set forth in the Recitals.

1.91 "**Other Component**" means one or more other devices or components.

1.92 "**Outstanding CMO Balance**" has the meaning set forth in Section 11.5 (Working Capital Fund).

1.93 "**Party**" and collectively "**Parties**" has the meaning set forth in the Preamble.

1.94 "**Patents**" means (a) all patents and patent applications in any country or jurisdiction in the Territory, and (b) any substitutions, divisions, continuations, continuations-in-part, reissues, renewals, registrations, confirmations, re-examinations, extensions, supplementary protection certificates, and the like.

1.95 "**Payors**" has the meaning set forth in Section 4.5 (Rebates).

1.96 "**PhRMA Code**" has the meaning set forth in Section 4.10.1 (Compliance).

1.97 "**Product Materials**" means any and all promotional materials, training materials, medical education materials, packaging and labeling, and all other literature or other information related to a Licensed Product.

1.98 "**Profit**" means, with respect to a Licensed Product in the Territory, the Net Sales or other revenue received for such Licensed Product in the Territory in a given period *minus* (a) an amount equal to [**] *plus* [**], *minus* (b) an amount equal to [**], and *minus* (c) [**].

1.99 "**Promote**," "**Promotion**," or "**Promoting**" means to market, detail, advertise, or otherwise promote a Licensed Product, but does not include the sale of, or Medical Affairs activities with respect to, such Licensed Product.

1.100 "**Quarterly Report**" has the meaning set forth in Section 11.6.2 (Quarterly Reports).

1.101 "**Recipient**" has the meaning set forth in Section 14.2 (Exceptions).

1.102 "**Regulatory Approval**" means any NDA approval by the FDA.

1.103 "**Regulatory Filings**" means all applications, filings, dossiers, and other documents submitted to the FDA in support of research or development of the Licensed Compound and the Licensed

Products, including for the purpose of obtaining Regulatory Approval from the FDA. Regulatory Filings will include all INDs and NDAs.

1.104 "**Reimbursement Date**" means the later of (a) the date on which a HCPCS Code has been issued by CMS for the Licensed Product and is effective for billing or (b) date on which CMS determines that the Licensed Product is either (i) to be reimbursed using the TDAPA, (ii) included as part of the ESRD PPS Bundled Payment System, or (iii) included under Medicare Part D.

1.105 "**Relevant Factors**" means the following factors that may affect the research, development, Regulatory Approval, manufacturing, or commercialization of a Licensed Product (without taking into account any other product or products that Akebia or its Affiliates may be developing, manufacturing, or commercializing): actual issues of safety, efficacy, or stability; product profile (including product modality, category and mechanism of action); stage of development or life cycle status; actual and projected research, development, Regulatory Approval, manufacturing, and commercialization costs; issues regarding the ability to manufacture or have manufactured any Licensed Product; the likelihood of obtaining Regulatory Approvals for any Licensed Product in the Territory and the timing of such Regulatory Approvals; the labeling and anticipated labeling of such Licensed Product; past performance of such Licensed Product or similar products; present and future market potential of such Licensed Product; existing or projected pricing, sales, reimbursement, and profitability of such Licensed Product; pricing or reimbursement changes in relevant countries in the Territory; and proprietary position, strength, and duration of patent protection and anticipated exclusivity of such Licensed Product; and other relevant scientific, technical, operational, and commercial factors.

1.106 "**Safety Data**" has the meaning set forth in Section 12.2 (Adverse Drug Events).

1.107 "**Safety Stock Amount**" has the meaning set forth in Section 11.5 (Working Capital Fund).

1.108 "**Sale Transaction**" has the meaning set forth in Section 18.2 (Standstill).

1.109 "**Second Amended Agreement**" has the meaning set forth in the Preamble.

1.110 "**Specialty Pharmacy**" means those specialty pharmacies identified on Schedule 5.10 under the heading "Specialty Pharmacies" (as the same may be updated from time to time in accordance with Section 5.10 (Licensee Supply Group)) that provide pharmaceutical products to dialysis patients of Authorized Dialysis Centers. As of the Effective Date, "Specialty Pharmacies" includes FreseniusRx.

1.111 "**Statistically Significant**" means a p-value less than [**].

1.112 "**Stock Purchase Agreement**" means that certain Investment Agreement, dated as of the Effective Date, by and between Akebia and Licensee.

1.113 "**Sub-Committee**" has the meaning set forth in Section 2.4.1 (Sub-Committees).

1.114 "**Supply Agreement**" has the meaning set forth in Section 10.2 (Commercial Supply Agreement).

1.115 "**Suspension Period**" has the meaning set forth in Section 3.2.2 (Suspension).

1.116 "**Tail Period**" has the meaning set forth in Section 16.10.1 (Termination Fee).

1.117 "**TDAPA**" means Medicare's transitional drug add-on payment adjustment as defined under 42 CFR § 413.234(c) and as amended in the Federal Register / Vol. 83, No. 220 / November 14, 2018 and in effect as of the Effective Date.

1.118 "**Term**" has the meaning set forth in Section 16.1 (Term).

1.119 "**Termination Fee**" has the meaning set forth in Section 16.10.1 (Termination Fee).

1.120 "**Territory**" means the United States of America and its possessions, including Puerto Rico.

1.121 "**Third Party**" means any person or entity other than a Party or its Affiliates.

1.122 "**Third Party Dialysis Organization**" (or "**TPDO**") means a Third Party identified on Schedule 5.10 under the heading "Third Party Dialysis Organizations" (as the same may be updated from time to time in accordance with Section 5.10 (Licensee Supply Group)) that owns TPDO Clinics and has entered into a Licensee-TPDO Purchase Agreement meeting the requirements set forth in Section 5.3 (Licensee-TPDO Purchase Agreements).

1.123 "**TIW Modify Trial**" means that certain Clinical Trial referred to as the Phase 3b, Randomized, Open-label, Active-controlled Trial Evaluating the Efficacy and Safety of Oral Vadadustat Once Daily (QD) and Three Times Weekly (TIW) for the Maintenance Treatment of Anemia in Hemodialysis Subjects Converting from Erythropoiesis-Stimulating Agents (ESAs), Protocol No. 404-201-00012.

1.124 "**Total Working Capital Requirement**" has the meaning set forth in Section 11.5 (Working Capital Fund).

1.125 "**TPDO Clinics**" means the dialysis clinics (including home dialysis programs) owned by TPDOs in the Territory that are identified on Schedule 5.10 under the heading "TPDO Clinics" (as the same may be updated from time to time in accordance with Section 5.10 (Licensee Supply Group)).

1.126 "**Transfer Price**" has the meaning set forth in Section 11.4 (Transfer Price).

1.127 "**True-Up Amount**" has the meaning set forth in Section 4.5 (Rebates).

1.128 "**Upfront Payment**" has the meaning set forth in Section 11.2 (Upfront Payment).

1.129 "**U.S.**" means the United States of America and its territories and possessions, including Puerto Rico.

1.130 "**Valid Claim**" means (a) a claim in any issued and unexpired Akebia Patent in the Territory, which claim has not been held invalid or unenforceable by a non-appealed or un-appealable decision of a court or Governmental Authority or other appropriate body of competent jurisdiction and has not been admitted invalid or unenforceable through reissue, reexamination, or disclaimer, or has not been made unenforceable due to failure to pay maintenance fees; or (b) a claim in any pending Akebia Patent in the Territory that has not been abandoned or finally disallowed without the possibility of appeal or re-filing of the application; *provided that* such claim has not been pending more than seven years from the priority date of such application (but if such pending claim with a pendency of seven years or longer subsequently issues it will be considered a Valid Claim upon issuance). "Valid Claim" does not include any claim in any issued and unexpired Akebia Patent in the Territory Covering an alternative manufacturing process to produce the Licensed Compound or a Licensed Product, including its components (*i.e.*, a manufacturing process other than the manufacturing process used to produce the Licensed Compound or a Licensed Product as of the Effective Date).

1.131 "**VFMCRP**" has the meaning set forth in the Recitals.

1.132 "**Working Capital Fund**" has the meaning set forth in Section 11.5 (Working Capital Fund).

1.133 "**Working Capital Payment**" has the meaning set forth in Section 11.5 (Working Capital Fund).

Article 2

GOVERNANCE

2.1. Formation and Purpose of Coordination Committee. Licensee and Akebia will establish the coordination committee ("**Coordination Committee**"), which committee will coordinate and oversee the Parties' activities hereunder and have the additional responsibilities provided for herein. The Coordination Committee will dissolve upon the expiration of the Term. Each Party will designate up to three representatives with appropriate knowledge and expertise to serve as members of the Coordination Committee. Each Party may replace its Coordination Committee representatives at any time upon written notice to the other Party.

2.2. Meetings. The Coordination Committee will hold meetings at such times as it elects to do so, but in no event will such meetings be held less frequently than [**] per calendar year, and such meetings may be held by audio or video teleconference. Other employees of each Party involved in activities under this Agreement may attend meetings of the Coordination Committee as participants, and, with the consent of each Party, consultants, representatives, or advisors involved in the same activities may attend meetings of the Coordination Committee as observers; *provided*, *however*, that such Third Party participants and observers are under legally binding obligations of confidentiality and non-use applicable to the Confidential Information of each Party that are at least as stringent as those set forth in Article 14 (Confidentiality).

2.3. Specific Responsibilities of the Coordination Committee. The Coordination Committee will:

2.3.1 coordinate the activities of the Parties hereunder;

2.3.2 [**] a Party's indication of interest in having [**], as described in [**];

2.3.3 [**] whether to add or remove any TPDO, GPO, IDO, or Authorized Dialysis Center to or from Schedule 5.10;

2.3.4 [**] any required revisions to this Agreement in response to any reimbursement system change or other rule change, as described under Section 4.6 (Reimbursement System and Other Changes);

2.3.5 [**] Akebia's initial Licensed Product Plan or any amendment or update thereto, or any matter related to the Licensed Product Plan referred to the Coordination Committee by either Party, as described under Section 4.7 (Licensed Product Plan);

2.3.6 [**] the Operational Plan and any amendment thereto, as described in Section 4.8 (Operational Plan);

2.3.7 [**] the implementation of the Operational Plan, as described in Section 4.8 (Operational Plan);

2.3.8 [**] the Parties' respective compliance programs, as described in Section 4.10 (Compliance)

2.3.9 [**] for the Parties to discuss matters relating to the Parties entering into arrangements with a given Specialty Pharmacy, as described in Section 4.11 (Specialty Pharmacies);

2.3.10 [**] conflicts raised by Licensee relating to Akebia's sales of Licensed Products to wholesalers or distributors, as described in Section 7.1 (Akebia Restrictions);

2.3.11 [**] whether to update the Working Capital Percentage, as described in Section 11.5 (Working Capital Fund);

2.3.12 [**] supply of the Licensed Products in the Territory;

2.3.13 perform such other functions as appropriate to further the purposes of this Agreement as determined by the Parties; and

2.3.14 receive at least on a [**] basis updates regarding Akebia's [**] of all Licensed Products for the DD-CKD Indication that are [**] as defined in this Agreement [**] in the Territory.

2.4. Other Committees.

2.4.1 Sub-Committees. If agreed by the Parties, the Coordination Committee may form sub-committees or working groups as may be necessary or desirable to facilitate the activities under this Agreement (each, a "**Sub-Committee**"). A Party may refer any dispute on a matter within a Sub-Committee's authority to the Coordination Committee for resolution. No such Sub-Committees' authority may exceed that specified for the Coordination Committee in this Article 2 (Governance).

2.4.2 Medical Affairs Committee. Without limiting the generality of, and subject to, the foregoing, following the Effective Date, the Parties will establish a Medical Affairs committee (the "**Medical Affairs Committee**") as a Sub-Committee. In addition to any other matters that the Coordination Committee may delegate to the Medical Affairs Committee, the Medical Affairs Committee will (a) [**] for the Parties to discuss and share information regarding the Parties' respective Medical Affairs activities for the Licensed Product in the Territory and (b) [**] any proposed investigator-initiated study for the Licensed Product in the Territory, as described in Section 4.9 (Medical Affairs Activities).

2.5. Dispute Resolution. Any decisions by the Coordination Committee [**], with each Party having one vote collectively through its representative members of the Coordination Committee, *provided* that a quorum must be present for any decision to be made by the Coordination Committee. The Coordination Committee will use good faith efforts to promptly resolve any such matter for which it has authority. If, after the use of good faith efforts, the Coordination Committee is unable to resolve any matter that is within the scope of the Coordination Committee's authority or any other disagreement between the Parties that the Parties may agree to refer to the Coordination Committee, in each case, within a period of [**], then a Party may refer such matter for resolution in accordance with Section 17.1 (Executive Officers).

Article 3

LICENSE GRANT

3.1. Grant of License to Licensee. Subject to the terms and conditions of this Agreement (including Section 3.2 (Effectiveness and Suspension), Section 3.3 (No Implied Rights), and Section 7.1 (Akebia Restrictions)), Akebia hereby grants to Licensee non-sublicensable, non-transferrable, license under the Akebia Technology to (a) sell the Licensed Products solely to the Licensee Supply Group, (b) sell the Licensed Products to Designated Wholesalers solely for resale to members of the Licensee Supply Group, and (c) conduct Medical Affairs with respect to the Licensed Product solely in accordance with Section 4.9 (Medical Affairs Activities), in each case ((a) through (c)), in the Territory in the Field during the Term, subject to the limitations set forth in Section 3.2 (Effectiveness and Suspension) (the "**License**"). The License will be exclusive (even as to Akebia) with respect to the foregoing clause (a) (regarding sales to the Licensee Supply Group for use in the Field in the Territory) and clause (b) (regarding sales to the Designated Wholesalers for resale solely to the Licensee Supply Group for use in the Field in the Territory), and co-exclusive (with Akebia) with respect to clause (c) (regarding the conduct of Medical Affairs in the Territory).

3.2. Effectiveness and Suspension.

3.2.1 **Effectiveness**. The License will be effective as of the Effective Date, *provided* that Licensee covenants and agrees that it will not sell or otherwise supply Licensed Products until the FDA has granted Regulatory Approval for a Licensed Product in the DD-CKD Indication in the Territory and (a) with respect to each particular Third Party Dialysis Organization, until such time as Licensee has entered into a Licensee-TPDO Purchase Agreement with such Third Party Dialysis Organization in accordance with Section 5.10.2 (Addition of TPDOs), (b) with respect to each particular IDO, until such time as Licensee has executed a Licensee-GPO Supplier Agreement with the GPO to which such IDO is a member and Licensee has entered into an IDO Participation Letter with such IDO in accordance with Section 5.7 (IDO Participation Letter), (c) with respect each particular Specialty Pharmacy, until such time as Licensee has entered into a Licensee- Specialty Pharmacy Supply Agreement with such Specialty Pharmacy in accordance with Section 5.4 (Terms of Licensee-Specialty Pharmacy Supply Agreement), and (d) with respect to each particular Designated Wholesaler, until such time as Licensee has entered into a Licensee-Designated Wholesaler Supply Agreement with such Designated Wholesaler in accordance with Section 5.8 (Terms of the Licensee-Designated Wholesaler Supply Agreements).

3.2.2 **Suspension**. Following the Effective Date, the License granted in Section 3.1 (Grant of License to Licensee), will remain in effect and exercisable by Licensee except during any period during which the License is suspended pursuant to Section 4.6 (Reimbursement System and Other Changes), or Section 16.7 (Termination or Suspension for Impacts on Pricing) (the "**Effective Period**"). During any period after the Effective Date during the Term that is not an Effective Period (a "**Suspension Period**"), the provisions set forth in Section 16.14 (Suspension of Licensed Rights) shall apply.

3.3. **New Dialysis Indication for Licensed Product.** In the event Akebia wishes to pursue an additional development program intended to support Regulatory Approval of the Licensed Product in an indication other than the DD-CKD Indication for the treatment of dialysis patients, the parties will discuss in good faith financial terms in support of such development program and commercialization of such new indication upon Regulatory Approval.

3.4. **Commercialization of Potential Combination Product(s).** In the event that Akebia develops any Combination Product for the DD-CKD Indication, then, no later than [**] following the NDA submission for such Combination Product, Licensee may notify Akebia of its desire to include such Combination Product under this Agreement. No later than [**] following Akebia's receipt of such notice, the Parties will discuss in good faith including such Combination Product under the definition of "Licensed Product" under this Agreement and any related amendments to this Agreement required with respect to the inclusion of such Combination Product hereunder, for a period of [**] (or such long period as the Parties may agree). If either (a) Licensee does not provide notice of its desire to include such Combination Product under this Agreement within such [**] period or (b) the Parties do not enter into a definitive amendment to this Agreement within the [**] negotiation period (as may be extended by agreement of the Parties), then, in each case ((a) and (b)), notwithstanding anything to the contrary set forth in this Agreement, Akebia will be free to exploit such Combination Product within and outside of the Field in the Territory, alone or with one or more Third Parties, without any further obligation to Licensee. Notwithstanding anything to the contrary set forth in this Agreement, following the [**] anniversary of the Effective Date, Akebia will have no further obligations and Licensee will have no further rights under this Section 3.4 (Commercialization of Potential Combination Product(s)).

3.5. **No Implied Right**s. Licensee will not practice the Akebia Technology or exploit the Licensed Compound or any Licensed Product other than as expressly licensed and permitted under this Agreement. Nothing in this Agreement will be interpreted to grant Licensee or any of its Affiliates any rights under any intellectual property rights owned or Controlled by Akebia or its Affiliates (including Akebia Technology) that are not expressly granted herein, whether by implication, estoppel, or otherwise. Any rights not expressly granted to Licensee by Akebia under this Agreement are hereby retained by Akebia. Without limiting the generality of the foregoing,

Akebia retains the exclusive right to sell Licensed Products to any Third Party outside of the Field.

Article 4

SALES OF LICENSED PRODUCTS

4.1. No Unauthorized Sales. Licensee will not, directly or indirectly, import, offer for sale, sell, or distribute the Licensed Compound or any Licensed Product (a) other than as expressly set forth in this Agreement in the Field in the Territory, (b) outside of the Territory, or (c) to any person or entity (i) other than the Licensee Supply Group or Designated Wholesalers or (ii) who uses or who Licensee reasonably expects will use such Licensed Product outside of the Field in the Territory. Licensee will promptly report to Akebia any unauthorized use, distribution, or transfer of the Licensed Compound or any Licensed Product in the Territory by or on behalf of any member of the Licensee Supply Group or any Designated Wholesaler, any of their respective Affiliates, or any distributor associated with any of the foregoing. Licensee will use Commercially Reasonable Efforts to stop any such unauthorized use, distribution, or transfer of such Licensed Compound or Licensed Product. In addition, if there is any unauthorized use, distribution, or transfer of any Licensed Product by any member of the Licensee Supply Group or any Designated Wholesaler, any of their respective Affiliates, or any distributor associated with any of the foregoing to a Third Party that is not a dialysis patient or Authorized Dialysis Center, then, if Licensee does not cause such unauthorized use, distribution, or transfer to cease or terminate the rights of the applicable member of the Licensee Supply Group or Designated Wholesaler, their Affiliates, or applicable distributor associated with any of the foregoing, in each case, within [**] of the date on which Licensee knows or should have known about such unauthorized use, distribution, or transfer, then the Parties will discuss in good faith an agreeable resolution for a period of [**]. If the Parties do not reach such a resolution during such [**] period, then Akebia may exercise its applicable right of termination with respect to such unauthorized use, distribution, or transfer pursuant to Section 16.4 (Termination for Unauthorized Sales).

4.2. Codes, Marks, and Packaging. Unless otherwise agreed by the Parties, the Licensed Products sold by Licensee to FKC, Specialty Pharmacies, IDOs, Third Party Dialysis Organizations, and Designated Wholesalers under this Agreement will not be resold or distributed under a different labeler code, product code, trade name, trademark, or packaging than units sold by Akebia outside of this Agreement or supplied by Akebia under this Agreement. Licensee will not change any such code, trade name, trademark, or packaging of any Licensed Product supplied to it under the Supply Agreement and will not affix any label or sticker on any Licensed Product without Akebia's prior written consent.

4.3. Promotion and Detailing. Akebia retains for itself and on behalf of its Affiliates and licensees (other than Licensee) the [**] right to Promote the Licensed Products, and Licensee and its Affiliates will not, and Licensee will ensure that the entities in the Licensee Supply Group and Designated Wholesalers do not, Promote any Licensed Product. If either Party desires [**], then such Party will provide such [**] to the other Party in writing and the Parties will [**] such [**] in the Territory through the Coordination Committee pursuant to Section 2.3.2 (Specific Responsibilities of the Coordination Committee). If Akebia agrees, [**], then Licensee will ensure that all such activities are conducted in compliance with the Licensee Compliance Program. Nothing in this Agreement will prohibit any entity in the Licensee Supply Group from including references to any Licensed Product or otherwise engaging in customary and routine clinical communications with their respective patient care staff regarding any Licensed Product or dosing regimens that include any Licensed Product. For the avoidance of doubt, unless otherwise agreed in writing by the Parties pursuant to this Section 4.3 (Promotion and Detailing), nothing in this Agreement will prevent Akebia or its Affiliates or licensees (other than Licensee) from Promoting any Licensed Product at any Authorized Dialysis Center.

4.4. Licensed Product Prices. To the fullest extent permitted by Applicable Law, Licensee will not, and will not knowingly permit its Affiliates, the Licensee Supply Group, or Designated

Wholesalers to, use or sell (as applicable) any Licensed Product in any manner that would result in [**]. In addition, to the fullest extent permitted by Applicable Law, in a written agreement with each of its Affiliates, any member of the Licensee Supply Group, or any Designated Wholesaler that receives any Licensed Product, Licensee will cause and require such Affiliates, member of the Licensee Supply Group, or Designated Wholesaler not to use or sell (as applicable) such Licensed Product in any manner that would result in [**]. For clarity, this Section 4.4 (Licensed Product Prices) will not prohibit (a) the Licensee Supply Group's customary dialysis clinic cost reporting to CMS and any other Governmental Authority, (b) a GPO's customary non-public disclosure of product pricing under GPO contracts solely to its member IDOs, or (c) any other disclosure required by Applicable Law.

4.5. **Rebates**. If Akebia receives a rebate invoice from (a) a state Medicaid program, (b) a state managed Medicaid entity, or (c) any other payor (collectively, "**Payors**") claiming a rebate on a unit of Licensed Product billed to a Payor for the treatment of a dialysis patient of an Authorized Dialysis Center, then Akebia shall pay such rebate and Licensee shall reimburse Akebia an equal amount. If interest or penalties are due on any such rebate, other than any interest or penalties attributable to Akebia's negligence or violation of Applicable Law, then Licensee shall reimburse such interest or penalties to Akebia and such amounts shall be deducted from Net Sales. No later than [**] following the end of each quarter after the Effective Date, Akebia will provide Licensee with a statement, in a format to be agreed upon by the Parties, identifying the units of Licensed Product provided for the treatment of a dialysis patient of an Authorized Dialysis Center for which Akebia paid rebates, interest, or penalties during such calendar quarter and the total amount of such rebates, interest, or penalties ("**True-Up Amount**"). Licensee will pay Akebia the True-Up Amount within [**] after receipt of such statement from Akebia.

4.6. **Reimbursement System and Other Changes**. In the event of a proposed rule change (a) to the TDAPA, (b) to the ESRD PPS Bundled Payment System, or (c) that Akebia [**] believes may impact the pricing of the Licensed Product outside of the Field, the Coordination Committee will [**] revisions to this Agreement, if any, in response to such proposed rule change. Following such discussion by the Coordination Committee, the Parties may [**] for the purpose of entering into a written amendment to this Agreement or such other changes to this Agreement as the Parties may agree. If such proposed rule change is not [**] to the TDAPA or the ESRD PPS Bundled Payment System as they exist as of the Effective Date (with respect to pricing or reimbursement of products like the Licensed Product), and if the Parties fail to enter into such a written amendment prior to the effectiveness of such rule change (unless the Parties agree in writing that no amendment is necessary), then Akebia may elect to suspend the License and commence a Suspension Period under Section 3.2.2 (Suspension), which Suspension Period will start no sooner than the effectiveness of such rule change and continue until the Parties enter into such an amendment.

4.7. **Licensed Product Plan**. [**], Akebia will prepare and submit to the Coordination Committee for its [**], pursuant to Section 2.3.9 (Specific Responsibilities of the Coordination Committee), a plan setting forth [**] (the "**Licensed Product Plan**"). The Licensed Product Plan may include information relating to [**]. In any event, the Licensed Product Plan must be [**]. The Parties, working through the Coordination Committee, will [**] the Licensed Product Plan, and Akebia will [**] into a revised Licensed Product Plan. During the Term, Akebia may prepare and submit to the Coordination Committee for its [**] amendments to the Licensed Product Plan on an as-needed basis, for example [**]. The Parties, working through the Coordination Committee, will [**] such amendments, and Akebia will give due consideration to and use good faith efforts to incorporate any reasonable recommendations of Licensee into such amendments.

4.8. **Operational Plan**. No later than [**] following Licensee's receipt of the Licensed Product Plan, Licensee will submit to the Coordination Committee, for [**], an operational plan for Licensee's and its Affiliates' launch, commercialization of, and Medical Affairs activities for the Licensed Product in the Field in the Territory (the "**Operational Plan**"). The Operational Plan will (a) allocate to Licensee operational roles and responsibilities consistent with those set forth on Schedule 4.8 (Operational Plan Roles and Responsibilities) and (b) include a [**] commercial forecast of its sales of Licensed Products in the Territory. The Operational Plan will be consistent

with the Licensed Product Plan in all respects. Prior to [**] during the Term, Licensee will provide an updated Operational Plan to the Coordination Committee for [**]. Licensee will negotiate the Licensee-FKC Supply Agreement, and any amendments thereto, each Licensee-Specialty Pharmacy Supply Agreement, and any amendments thereto, each Licensee-GPO Supplier Agreement, and any amendments thereto, each Licensee-TPDO Purchase Agreement, and any amendments thereto, and each Licensee-Designated Wholesaler Supply Agreement, and any amendments thereto, with the Licensee Supply Group and Designated Wholesalers, as applicable, in a manner consistent with the Operational Plan, to the extent applicable. During the Term, Licensee will commercialize the Licensed Product in accordance with the Operational Plan, and the Coordination Committee will review and monitor the implementation thereof to ensure coordination for successful launch and commercialization of the Licensed Product. Licensee may prepare and submit to the Coordination Committee for its [**] amendments to the Operational Plan on an as-needed basis and the Parties, working through the Coordination Committee, will [**] such amendments.

4.9. Medical Affairs Activities. Licensee will be responsible for conducting those Medical Affairs activities allocated to Licensee under the Operational Plan. Licensee will ensure that all such activities are conducted in compliance with Applicable Law and the Licensee Compliance Program. Licensee acknowledges that Akebia independently conducts certain activities, such as the funding of investigator-initiated studies if and as Akebia deems appropriate in accordance with its internal policies and procedures. In the event that any member of the Licensee Supply Group (excluding any Specialty Pharmacy) desires to conduct any investigator-initiated studies for the Licensed Product in the Territory in the Field and communicates such desire to Licensee, Licensee may submit a proposal on behalf of such member of the Licensee Supply Group to the Medical Affairs Committee, which will [**] such proposal.

4.10. Compliance.

4.10.1 As of the Effective Date and throughout the Term, Licensee will maintain and implement an effective healthcare compliance program that: (i) governs all employees and contractors; (ii) is consistent with the current U.S. Federal Sentencing Guidelines standards for effective compliance programs; (iii) complies with the then-current Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals (the "**PhRMA Code**"); and (iv) addresses standards applicable to activities within the scope of this Agreement, including the distribution and promotion of pharmaceutical products, adverse event reporting, data safeguards, privacy and protection (the "**Licensee Compliance Program**"). Licensee will send a current copy of any code, policies or other written materials comprising or documenting the Licensee Compliance Program to Akebia and provide Akebia with copies of any later updates. Such Licensee Compliance Program will be at least as comprehensive and contain standards at least as strict and up-to-date as those maintained by Akebia for its own equivalent activities for the Licensed Product and that, if the Licensee Compliance Program is not so comprehensive and up-to-date, then Licensee will ensure that all such sales and Medical Affairs activities are conducted in accordance with Akebia's compliance standards (as communicated to Licensee from time to time during the Term). Throughout the Term and with respect to the commercialization of Licensed Products under this Agreement, Licensee and each of its Affiliates will further operate in strict compliance with Applicable Law, the PhRMA Code, the Licensee Compliance Program and Akebia compliance standards, as applicable.

4.10.2 Throughout the Term, Licensee will maintain adequate systems, policies, and procedures to screen before hire and annually thereafter all prospective and current employees, contractors, subcontractors, or agents against (i) the List of Excluded Individuals/Entities compiled by the Office of the Inspector General in the Department of Health and Human Services, and (ii) the General Services Administration's List of Parties Excluded from Federal Programs. Such policies and procedures require Licensee's prospective and current employees, contractors, subcontractors, or agents to disclose immediately to Licensee any exclusion, debarment, suspension, or declaration of ineligibility from

participation in federal health care programs or in federal procurement or non-procurement programs and any investigation or indictment which may result in an exclusion, debarment, suspension, or declaration of ineligibility.

4.10.3 Throughout the Term, Licensee will maintain adequate systems, policies, and procedures to provide training to its employees on a regular basis, which includes training on the Licensee Compliance Program.

4.10.4 [**], the Coordination Committee will conduct a review of the Parties' respective compliance programs.

4.10.5 Licensee and its Affiliates will only use Product Materials that are prepared by Akebia, or otherwise approved in advance in writing by Akebia, in each case, in connection with its sale of such Licensed Products under this Agreement or any Medical Affairs activities with respect to the Licensed Product or any Promotion of any Licensed Product by Licensee in the Field in the Territory that may be agreed to by the Parties in accordance with Section 4.3 (Promotion and Detailing). Akebia will use Commercially Reasonable Efforts to ensure that the Product Materials meet all applicable requirements under the Federal Food, Drug, and Cosmetic Act and conform to applicable FDA regulations. In addition, Licensee will ensure that the entities in the Licensee Supply Group only use Product Materials that are consistent with those Product Materials prepared and provided by Akebia.

4.10.6 Each Party shall have responsibility for tracking and reporting payments or other transfers of value made directly or indirectly to health care professionals or other persons and entities under the so-called federal "sunshine law" or Open Payments (42 U.S.C. §1320a-7a) and analogous state laws in connection with the performance of this Agreement in accordance with their respective compliance policies

4.11. **Specialty Pharmacies**. Subject to Section 5.10.2 (Additions to Schedule 5.10), Licensee will use [**] to enter into and maintain supply agreements with specialty pharmacies to the extent necessary to make the Licensed Product available to all patients who receive dialysis at Authorized Dialysis Centers, and will ensure that the supply agreements that it enters into with Specialty Pharmacies meet the requirements set forth in Section 5.4 (Terms of the Licensee-Specialty Pharmacy Supply Agreements), Section 6.4 (No Effect on Licensed Product Reported Pricing), and Section 13.5.4. Notwithstanding anything to the contrary set forth in this Agreement, nothing herein will restrict Akebia from entering into a direct or indirect arrangement with any Specialty Pharmacy for the distribution of Licensed Products outside of the Field. In the event that the Parties each intend to enter into arrangements with the same Specialty Pharmacy, then the Parties will discuss such matter, along with any operational considerations, through the Coordination Committee.

Article 5

SUPPLY AGREEMENTS

5.1. **Licensee-FKC Supply Agreement**. Licensee has entered into a supply agreement with its Affiliate, VFMCRP, dated as of December 18, 2018, and in turn VFMCRP has entered into an identical supply agreement with FKC with an effective date of December 18, 2018, pursuant to which, after the Effective Date, Licensed Products will be sold by Licensee (either directly or indirectly through VFMCRP) to FKC in an arms-length transaction for use in Authorized Dialysis Centers, other than TPDO Clinics and IDO Clinics (together, the "**Licensee-FKC Supply Agreement**"), and only pursuant to such agreements.

5.1.1 **Initial Supply Agreement**. Licensee represents and warrants that the Licensee-FKC Supply Agreement satisfies the requirements of Section 5.2 (Terms of the Licensee-FKC Supply Agreement) with the exception of Section 5.2.8, and does not include any terms related to [**] of any Licensed Product. If the Licensee-FKC Supply Agreement is

terminated or expires, then Akebia may terminate this Agreement pursuant to Section 16.6 (Termination by Akebia for Failure to Enter Into or Amend the Licensee-FKC Supply Agreement or Licensee-FreseniusRx Supply Agreement).

5.1.2 **Amendment to Supply Agreement**. No later than [**] after the Reimbursement Date, Licensee (either directly or indirectly through VFMCRP) and FMCNA or any of its Affiliates (hereinafter referred to as "FMC Contracting Party") will amend the Licensee-FKC Supply Agreement to finalize such agreement in order to satisfy all requirements of Section 5.2 (Terms of the Licensee-FKC Supply Agreement) (to the extent such Licensee-FKC Supply Agreement does not already do so), including Section 5.2.8. If Licensee (either directly or indirectly through VFMCRP) and FMC Contracting Party do not enter into an amendment of such Licensee-FKC Supply Agreement during such [**] period, then Akebia may terminate this Agreement pursuant to Section 16.6 (Termination by Akebia for Failure to Enter Into or Amend the Licensee-FKC Supply Agreement or Licensee-FreseniusRx Supply Agreement). Licensee will provide notice to Akebia that the amendments described herein have been executed and delivered by the parties thereto no later than [**] after entering into such amendments, including whether such amendment satisfies the requirements of Section 5.2.8. Notwithstanding anything herein to the contrary, Licensee (or in case the Licensee-FKC Supply Agreement has been entered into by VFMCRP, then VFMCRP) may amend the Licensee-FKC Supply Agreement in such a way that it no longer complies with Section 5.2.8, if so agreed in writing by the Parties.

5.2. **Terms of the Licensee-FKC Supply Agreement**. Licensee will ensure that, throughout the Term, the Licensee-FKC Supply Agreement:

5.2.1 requires that FMC Contracting Party either (a) use [**] logistic service providers (each, an "**LSP**") and/or use a Designated Wholesaler to provide the Licensed Products solely to the Authorized Dialysis Centers (other than TPDO Clinics and IDO Clinics), in which arrangement the LSP will not own or take title to any Licensed Product, or (b) itself directly provide such Licensed Products solely to Authorized Dialysis Centers other than TPDO Clinics and IDO Clinics;

5.2.2 prohibits FMC Contracting Party from distributing or transferring Licensed Products to any person or entity other than (a) the LSPs or (b) Authorized Dialysis Centers that are not TPDO Clinics or IDO Clinics;

5.2.3 requires that FMC Contracting Party report any unauthorized use, distribution, or transfer of any Licensed Product promptly to Licensee;

5.2.4 names Akebia as an intended third party beneficiary of such Licensee-FKC Supply Agreement with respect to relevant and appropriate provisions of such agreement;

5.2.5 (a) prohibits FMCNA, FMCNA's Affiliates (including FKC), or Majority Owned Clinics from [**], except as required by Applicable Law), and (b) [**];

5.2.6 requires FMC Contracting Party to cause each Authorized Dialysis Center to (a) not distribute or transfer any Licensed Product to any person or entity other than a dialysis patient in the Field in the Territory or another Authorized Dialysis Center in the Territory, (b) use each Licensed Product, and implement reasonable measures to ensure that each Licensed Product is used only for (i) the treatment of dialysis patients in the Field in the Territory, and (ii) delivering clinical treatment consistent with the requirements of Section 4.4 (Licensed Product Prices) and to dialysis patients in the Field in the Territory; (c) report any unauthorized use, distribution, or transfer of any Licensed Product promptly to Licensee; and (d) [**], except as required by Applicable Law and to promptly inform Licensee, FMC Contracting Party, and Akebia if the Authorized Dialysis Center believes that it is required by Applicable Law [**];

5.2.7 contains such additional provisions as may be necessary to ensure Licensee's compliance with the terms set forth in this Agreement;

5.2.8 requires that Licensed Products be sold by Licensee (either directly or indirectly through VFMCRP) to FMC Contracting Party in an arms-length transaction, and by FMC Contracting Party directly (or indirectly through FKC or FreseniusRx) to patients who receive dialysis at Authorized Dialysis Centers; and

5.2.9 in case the Licensee-FKC Supply Agreement includes sales to FreseniusRx, then sub-sections 5.4.1 and 5.4.6 shall be applicable to the Licensee-FKC Supply Agreement.

5.3. Licensee-FreseniusRx Supply Agreement. Licensee has entered into a supply agreement with its Affiliate VFMCRP dated as of December 18, 2018, and in turn, in the event the Licensee-FKC Supply Agreement does not include sales to FreseniusRx, VFMCRP will enter into a separate supply agreement with FreseniusRx, or an amendment thereto, pursuant to which, after the Effective Date, Licensed Products will be sold by Licensee (either directly or indirectly through VFMCRP) to FreseniusRx in an arms-length transaction, and by FreseniusRx directly to patients who receive dialysis at Authorized Dialysis Centers (together, the "**Licensee-FreseniusRx Supply Agreement**") in compliance with the requirements of Section 5.4 (Terms of the Licensee-Specialty Pharmacy Supply Agreements). If, in the event the Licensee-FKC Supply Agreement does not include sales to FreseniusRx, and Licensee, VFMCRP, and FreseniusRx do not enter into such an agreement or amendment, as applicable, within [**] after the Reimbursement Date, then Akebia may terminate this Agreement pursuant to Section 16.6 (Termination by Akebia for Failure to Enter Into or Amend the Licensee-FKC Supply Agreement or Licensee-FreseniusRx Supply Agreement). Licensee will provide notice to Akebia no later than [**] after entering into such agreement or amendment, as applicable. Notwithstanding anything herein to the contrary, Vifor may terminate the Licensee-FreseniusRx Supply Agreement if so agreed in writing by the Parties.

5.4. Terms of the Licensee-Specialty Pharmacy Supply Agreements. In addition to the Licensee-FreseniusRx Supply Agreement, Licensee (either directly or indirectly through VFMCRP) will enter into supply agreements with each other Specialty Pharmacy pursuant to which Licensee will sell Licensed Products directly to such Specialty Pharmacy in arms-length transactions for use by patients who receive dialysis at Authorized Dialysis Centers or at home from an Authorized Dialysis Center (together with the Licensee-FreseniusRx Supply Agreement, each such supply agreement, a "**Licensee-Specialty Pharmacy Supply Agreement**"), and only pursuant to such agreement. Licensee will ensure that, throughout the Term, each Licensee-Specialty Pharmacy Supply Agreement with each Specialty Pharmacy:

5.4.1 prohibits the Specialty Pharmacy from distributing or transferring Licensed Products to any person or entity other than to dialysis patients for treatment;

5.4.2 requires that the Specialty Pharmacy report any unauthorized use, distribution, or transfer of any Licensed Product promptly to Licensee;

5.4.3 requires the Specialty Pharmacy to (a) implement reasonable measures to ensure that each Licensed Product is used only for (i) the treatment of dialysis patients in the DD-CKD Indication, and (ii) delivering treatment consistent with the requirements of Section 4.4 (Licensed Product Prices); (b) report any unauthorized use, distribution, or transfer of any Licensed Product promptly to Licensee and Akebia; and (c) [**], except as required by Applicable Law, and to promptly inform Licensee and Akebia if the Specialty Pharmacy believes that it is required by Applicable Law [**];

5.4.4 prohibits the Specialty Pharmacy from [**], except as required by Applicable Law;

5.4.5 names Akebia as an intended third party beneficiary of such Licensee-Specialty Pharmacy Supply Agreement with respect to relevant and appropriate provisions of such agreement;

5.4.6 prohibits the Specialty Pharmacy from changing any labeler code, product code, trade name, trademark, or packaging of any Licensed Product supplied to it under the Licensee-Specialty Pharmacy Supply Agreement and from affixing any label or sticker on any Licensed Product;

5.4.7 contains such additional provisions as may be necessary to ensure such Specialty Pharmacy's compliance with the terms set forth in this Agreement.

5.5. Licensee-TPDO Purchase Agreements. Licensee will enter into purchase agreements with each Third Party Dialysis Organization pursuant to which, after the Effective Date, Licensee will sell Licensed Products in arms-length transactions to such Third Party Dialysis Organizations for use in TPDO Clinics (each such supply agreement, a "**Licensee-TPDO Purchase Agreement**"), and only pursuant to such agreement. Licensee will ensure that, throughout the Term, each Licensee-TPDO Purchase Agreement with each Third Party Dialysis Organization:

5.5.1 requires that the Third Party Dialysis Organization itself directly provide Licensed Products solely to TPDO Clinics that have been approved by Akebia as provided in Section 5.10 (Licensee Supply Group);

5.5.2 prohibits the Third Party Dialysis Organization from distributing or transferring Licensed Products to any person or entity other than TPDO Clinics approved by Akebia as provided in Section 5.10 (Licensee Supply Group);

5.5.3 requires that the Third Party Dialysis Organization report any unauthorized use, distribution, or transfer of any Licensed Product promptly to Licensee;

5.5.4 names Akebia as an intended third party beneficiary of such Licensee-TPDO Purchase Agreement with respect to relevant and appropriate provisions of such agreement;

5.5.5 (a) prohibits the Third Party Dialysis Organization and its TPDO Clinics from [**], except as required by Applicable Law, and (b) [**];

5.5.6 requires the Third Party Dialysis Organization to (a) not distribute or transfer any Licensed Product to any person or entity other than a dialysis patient in the Field in the Territory or a TPDO Clinic in the Territory, (b) use each Licensed Product, and implement reasonable measures to ensure that each Licensed Product is used only for (i) the treatment of dialysis patients in the Field in the Territory, and (ii) delivering clinical treatment consistent with the requirements of Section 4.4 (Licensed Product Prices); (c) report any unauthorized use, distribution, or transfer of any Licensed Product promptly to Licensee; and (d) [**], except as required by Applicable Law and to promptly inform Licensee, the Third Party Dialysis Organization, and Akebia if such Third Party Dialysis Organization or any of its TPDO Clinics believes that it is required by Applicable Law [**];

5.5.7 permits Akebia to (a) take assignment of the Licensee-TPDO Purchase Agreement in the event this Agreement is terminated by Licensee pursuant to Section 16.9 (Termination for Convenience) and (b) take over Licensee's supply of Licensed Products under the Licensee-TPDO Purchase Agreement pursuant to Section 16.15 (Suspension of Licensed Rights) in the event of a Suspension Period; and

5.5.8 contains such additional provisions as may be necessary to ensure Licensee's compliance with the terms set forth in this Agreement.

5.6. Licensee-GPO Supplier Agreement. Licensee will enter into a supplier agreement with each GPO pursuant to which, after the Effective Date, Licensee will sell Licensed Products in arms-length transactions solely to the IDO members of such GPO via a distributor associated with such GPO (such supplier agreement, the "**Licensee-GPO Supplier Agreement**"), and only pursuant to such agreement. Licensee will ensure that, throughout the Term, each Licensee-GPO Supplier Agreement:

5.6.1 requires that the GPO and its associated distributor provide Licensed Products solely to the GPO's member IDOs that have executed an IDO Participation Letter with Licensee in accordance with Section 5.7 (IDO Participation Letter);

5.6.2 prohibits the GPO and any of its associated distributors from distributing or otherwise transferring Licensed Products to any person or entity other than the GPO's member IDOs that have executed an IDO Participation Letter with Licensee in accordance with Section 5.7 (IDO Participation Letter);

5.6.3 requires the GPO to cause any member independent operator of dialysis clinics that desires to obtain Licensed Products through such GPO to execute an IDO Participation Letter containing the terms set forth in Schedule 5.7 prior to receiving any Licensed Product through such GPO or its associated distributor;

5.6.4 requires that the GPO report any unauthorized use, distribution, or transfer of any Licensed Product promptly to Licensee;

5.6.5 (a) with the exception of price disclosure by the GPO to its member IDOs, prohibits the GPO and IDOs from [**], except as required by Applicable Law, and (b) [**];

5.6.6 requires the GPO to implement reasonable measures to ensure that each Licensed Product is used only for (a) the treatment of dialysis patients in the Field in the Territory, and (b) delivering clinical treatment consistent with the requirements of Section 4.4 (Licensed Product Prices);

5.6.7 names Akebia as an intended third party beneficiary of such Licensee-GPO Supplier Agreement with respect to relevant and appropriate provisions of such agreement;

5.6.8 permits Akebia to take assignment of the Licensee-GPO Supplier Agreement in the event this Agreement is terminated by Licensee pursuant to Section 16.9 (Termination for Convenience) and (b) take over Licensee's supply of Licensed Products under the Licensee-GPO Supply Agreement pursuant to Section 16.15 (Suspension of Licensed Rights) in the event of a Suspension Period; and

5.6.9 contains such additional provisions as may be necessary to ensure Licensee's compliance with the terms set forth in this Agreement.

5.7. IDO Participation Letter. Licensee will cause each GPO to require any member IDO that desires to obtain Licensed Products through such GPO to enter into an IDO Participation Letter with Licensee containing the terms set forth in Schedule 5.7, as a condition of such IDO purchasing Licensed Products through such GPO.

5.8. Terms of the Licensee-Designated Wholesaler Supply Agreements. Licensee will enter into supply agreements with each Designated Wholesaler pursuant to which Licensee will sell Licensed Products to such Designated Wholesaler in arms-length transactions solely for sale by such Designated Wholesaler to a member of the Licensee Supply Group other than as Designated Wholesaler (each such supply agreement, a "**Licensee- Designated Wholesaler Supply Agreement**"), and only pursuant to such agreement. Licensee will ensure that, throughout the Term, each Licensee-Designated Wholesaler Supply Agreement with each Designated Wholesaler:

5.8.1 requires that such Designated Wholesaler provide Licensed Products solely to members of the Licensee Supply Group under an exclusive distribution account / "chargeback" sales model;

5.8.2 prohibits such Designated Wholesaler from distributing or transferring Licensed Products to any person or entity other a member of the Licensee Supply Group;

5.8.3 requires that such Designated Wholesaler report any unauthorized use, distribution, or transfer of any Licensed Product promptly to Licensee;

5.8.4 prohibits such Designated Wholesaler from changing any labeler code, product code, trade name, trademark, or packaging of any Licensed Product supplied to it under the Licensee-Designated Wholesaler Supply Agreement and from affixing any label or sticker on any Licensed Product; and

5.8.5 contains such additional provisions as may be necessary to ensure such Designated Wholesaler's compliance with the terms set forth in this Agreement.

In addition, Licensee will use reasonable efforts to ensure that each Licensee-Designated Wholesaler Supply Agreement with each Designated Wholesaler names Akebia as an intended third party beneficiary of such Licensee-Designated Wholesaler Supply Agreement.

5.9. Akebia's Right to Review Agreements. Upon request, Licensee further agrees to permit (a) an independent auditor or law firm selected by Akebia and approved by Licensee (which approval will not be unreasonably withheld or delayed) or (b) Akebia, upon Licensee's approval (which may be withheld in its sole discretion), to examine the Licensee-FKC Supply Agreement, each Licensee-Specialty Pharmacy Supply Agreement, each Licensee-GPO Supplier Agreement, each Licensee-TPDO Purchase Agreement, each Licensee-Designated Wholesaler Supply Agreement, and each IDO Participation Letter, or other agreements between Licensee and any member of the Licensee Supply Group, regarding a Licensed Product, in each case, solely to ensure that such agreements are consistent with the terms set forth in this Agreement. In the event that Akebia is the reviewing party, then Licensee may redact sensitive commercial information from any such agreement to the extent not necessary for Akebia to determine whether such agreement is consistent with the terms set forth in this Agreement. Any such auditor or law firm will be bound by a legal agreement obligating it to maintain the confidentiality of such information and not to share such information with Akebia or any other person. Any such auditor or law firm will summarize its findings solely by stating whether or not such agreements are consistent with Licensee's obligations hereunder, and if such agreements are inconsistent with Licensee's obligations, identify such inconsistencies to Akebia. Such examination will not be performed more than once per calendar year. Akebia will be responsible for the expenses incurred in connection with such examination, except in the event that the results of any examination reveal that such agreements are materially inconsistent with the terms set forth in this Agreement, in which case reasonable fees for such examination will be paid by Licensee.

5.10. Licensee Supply Group.

5.10.1 List of Licensee Supply Group. As of the Effective Date, listed on Schedule 5.10 are (a) all of the Authorized Dialysis Centers (including each FKC Clinic and Majority Owned Clinic, which are each separately identified on Schedule 5.10), (b) each Third Party Dialysis Organization and each TPDO Clinic owned by each such Third Party Dialysis Organization, (c) each GPO, (d) each IDO that has executed an IDO Participation Letter and the IDO Clinics of each such IDO, and (f) the Specialty Pharmacies. Licensee will provide to the Coordination Committee an updated Schedule 5.10 [**], and on the Effective Date.

5.10.2 Additions to Schedule 5.10. In the event Licensee wishes to update Schedule 5.10 to include any entity within the Licensee Supply Group that has not been previously listed on Schedule 5.10, [**], Licensee will promptly provide to the Coordination Committee

an updated Schedule 5.10 that the applicable entity under the applicable heading on Schedule 5.10; and *provided further* that the License granted in Section 3.1 (Grant of License to Licensee) will only become exercisable by Licensee with respect to such entity, and such entity will only be considered a member of the Licensee Supply Group for purposes of this Agreement, when Licensee has entered into a supply agreement with such entity in accordance with the applicable provisions of this Article 5 (Supply Agreements). and only for so long as such supply agreement remains in effect.

5.10.3 Removal of Licensee Supply Group Members by Akebia. Akebia may provide written notice to Licensee that Akebia proposes to remove any member of the Licensee Supply Group from Schedule 5.10 in the event that such member of the Licensee Supply Group (a) has not sold any Licensed Product within [**] of its inclusion on Schedule 5.10, (b) has not sold any Licensed Product over a consecutive period of at least [**], or (c) in the case of any IDO, does not have access to one or more of Licensee's marketed products, other than the Licensed Product, through a GPO of which such IDO is a member. Within [**] following Licensee's receipt of a written notice that Akebia proposes to remove an Authorized Dialysis Center from Schedule 5.10, which shall explain the reasons therefore, Licensee may object to such removal in writing, following which the Parties will discuss in good faith an agreeable resolution within [**]. If the Parties do not reach such a resolution during such [**] period, then Akebia may remove such member of the Licensee Supply Group from Schedule 5.10, and in such event Licensee will promptly stop the supply of Licensed Products to such member of the Licensee Supply Group.

5.10.4 Schedule 5.9. [**] the Third Party Dialysis Organizations and their TPDO Clinics and (b) the GPOs, IDOs, and their IDO Clinics, as each ((a) and (b)) are set forth on Schedule 5.10 hereto as of the Effective Date. Licensee represents and warrants that the updated version of Schedule 5.10 attached hereto is accurate and complete as of the Effective Date.

Article 6

PRICING AND PRICE REPORTING

6.1. Pricing. Other than with respect to (a) the Licensee Supply Group's customary dialysis clinic cost reporting to CMS and any other Governmental Authority, (b) a GPO's customary non-public disclosure of product pricing under GPO contracts solely to its member IDOs that have executed an IDO Participation Letter, or (iii) disclosures required by law, Licensee will not, will cause its Affiliates not to, and will require the Licensee Supply Group and Designated Wholesalers not to, disclose [**], and in each case, such information will be Confidential Information subject to the terms of Article 14 (Confidentiality).

6.2. Intention Regarding Impacts on Pricing. Akebia intends, and enters into this Agreement in reliance upon, the Agreement and the supply of Licensed Product by Akebia to Licensee under the Supply Agreement not giving rise to, or otherwise affecting, [**]. Notwithstanding the foregoing, if the administration of a Licensed Product by an Authorized Dialysis Center or Specialty Pharmacy to a dialysis patient gives rise to a rebate obligation under the Medicaid Drug Rebate Program or the Public Health Service Act Section 340B Drug Discount Program, then so long as (a) Licensee reimburses Akebia in accordance with Section 4.5 (Rebates) for any such rebate obligation incurred by Akebia and (b) such rebate does not affect the AMP, Best Price, 340B Ceiling Price, ASP, or NFAMP of any Akebia product outside of the Field or otherwise contravene Section 6.4 (No Effect on Licensed Product Reported Pricing), then such rebate obligation will not violate the intent of this Section 6.2 (Intention Regarding Impacts on Pricing).

6.3. Impacts on Pricing. If, at any time, (a) there has been a breach of Section 6.1 (Pricing) or Section 6.4 (No Effect on Licensed Product Reported Pricing), (b) through the actions by or on behalf of Licensee, any of its Affiliates, any Designated Wholesaler, or any member of the Licensee Supply Group [**], and even if such actions do not constitute a breach by Licensee

under Section 4.4 (Licensed Product Prices)), [**], or (d) [**], then, in each case ((a) through (d)), without limiting Akebia's other rights and remedies under this Agreement, the Parties will [**] an agreeable resolution for a period of [**]. If the Parties do not reach such a resolution during such [**] period, then Akebia may suspend the License or terminate this Agreement pursuant to Section 16.7 (Termination or Suspension by Akebia for Impacts on Pricing).

6.4. **No Effect on Licensed Product Reported Pricing**. Licensee will, will cause its Affiliates to, and will require the Licensee Supply Group and Designated Wholesalers to, use and sell (as applicable) each Licensed Product solely in the Field in the Territory. To the fullest extent permitted by Applicable Law, Licensee and its Affiliates will not use, sell, transfer, or distribute the Licensed Product (a) to any "Retail Community Pharmacy" (as defined in 42 U.S.C. § 1396r- 8(k)(10)); or (b) to any other customer, or in any manner, that would cause such sale, transfer, or distribution to affect the AMP, Best Price, 340B Ceiling Price, ASP, or NFAMP of any Akebia product. Licensee will provide prompt written notice to Akebia if Licensee or any of its Affiliates uses, sells, transfers, or distributes any Licensed Product in violation of this Section 6.4 (No Effect on Licensed Product Reported Pricing).

For the avoidance of doubt, the Parties acknowledge and agree that FreseniusRx does not meet the definition of a "Retail Community Pharmacy" under 42 U.S.C. § 1396r-8(k)(10) and implementing regulations.

Article 7

EXCLUSIVITY

7.1. **Akebia Restrictions**. During the Effective Period, Akebia will not, and will cause its Affiliates and licensees (other than Licensee) to not, sell any Licensed Product directly to any member of the Licensee Supply Group for any use in the Field in the Territory; *provided*, *however*, that (a) Akebia will not be required to prohibit any Third Party wholesaler or distributor (including any Designated Wholesaler) from selling any Licensed Product to the Licensee Supply Group and (b) Akebia will not be prohibited from selling Licensed Products to any member of the Licensee Supply Group for any use outside of the Field. In the event that Licensee reasonably believes any sales of Licensed Products by wholesalers or distributors generates conflicts in Licensee's distribution of Licensed Products, then Licensee may raise such conflict at the Coordination Committee, and Akebia will consider, if feasible, whether steps can be taken with such wholesaler or distributor to address such conflict.

7.2. **Licensee Restrictions**. Without the prior written consent of Akebia, neither Licensee nor any of its Affiliates will directly or indirectly Promote, sell, or have sold, or enter into any agreement to Promote, sell, or have sold, any Competing Product in the Territory to FKC, any entity in or member of the Licensee Supply Group, any Designated Wholesaler, or any Authorized Dialysis Center. Notwithstanding the foregoing, if [**].

Article 8

REGULATORY

Akebia will use Commercially Reasonable Efforts to (a) prepare the NDA in the Territory for each Licensed Product based on its global development plan for such Licensed Product, and (b) obtain and maintain Regulatory Approval in the DD-CKD Indication in the Territory for each Licensed Product. Akebia will be responsible for preparing, filing, and submitting, directly or through its Affiliates or licensees, all Regulatory Filings and correspondence with the applicable regulatory authorities for each Licensed Product at its sole cost and expense.

Article 9

TRADEMARKS; NAMES

9.1. Trademark Responsibility. Akebia will be responsible for (a) registering, prosecuting, maintaining, and enforcing the Akebia Trademarks in the Territory, (b) preparing any guidelines applicable to the use of the Akebia Trademarks, and (c) investigating and defending any infringement or threatened infringement relating to any of the foregoing, in each case, at its sole cost and expense. Licensee will cooperate and assist Akebia with any of the foregoing activities with respect to all Akebia Trademarks, including, if requested by Akebia, providing any specifications, affidavits, declarations, or other documents necessary for Akebia to submit to appropriate Governmental Authorities in order to register and prosecute the Akebia Trademarks. Akebia will own and be responsible for securing any domain names associated with the Akebia Trademarks, and will be responsible for the costs associated with protecting such domain names. Neither Licensee nor any of its Affiliates will obtain or hold any such domain name in its own name.

9.2. Trademark License. Subject to the terms and conditions of this Agreement, effective as of the Effective Date, Akebia hereby grants and will grant to Licensee and its Affiliates a non-exclusive non-sublicensable, non-transferrable, royalty-free license to use the Akebia Trademarks solely in connection with the sale, and, [**], of the Licensed Products in the Field in the Territory in accordance with this Agreement. Licensee will maintain the quality of the Licensed Products in accordance with this Agreement and the Supply Agreement. Licensee additionally will assure at all times that the Licensed Products are sold in accordance with Applicable Law.

9.3. Trademark Ownership and Cooperation. Each Party acknowledges that Akebia has sole and exclusive ownership of all rights, title, and interests in and to the Akebia Trademarks. Licensee will not, and will cause its Affiliates and the entities in the Licensee Supply Group not to, register in their own name any trademark, corporate name, domain name, social media account, or other source identifier containing any trademark owned by Akebia or any word or mark that is confusingly similar to any such trademark. All use of any Akebia Trademark and all goodwill and benefit arising from such use will inure to the sole and exclusive benefit of Akebia. Licensee will place and display the Akebia Trademarks on and in connection with the Licensed Products only in such form and manner as specified in the guidelines adopted from time-to-time by Akebia and provided to Licensee. Except as otherwise expressly provided in this Agreement, Licensee is not granted any license under, and will not use, any trademarks of Akebia in connection with any Licensed Product.

9.4. Defense of Third Party Infringement Claims.

9.4.1 Notice; Akebia Initiation. Licensee will immediately provide written notice to Akebia if a Third Party asserts that a Patent or other right controlled by such Third Party is or will be infringed by Licensee's activities under this Agreement or Licensee becomes aware of a Patent or other right that might form the basis for such a claim, which notice will include all facts related to such claim in reasonable detail. [**].

9.4.2 Right to Defend. If, during the Term of the Agreement, a Third Party asserts that a Patent or other right controlled by such Third Party is infringed or will be infringed in the Territory by Licensee's exercise of the rights granted to it under this Agreement, then:

(a) [**] in the Territory, [**] will defend [**] against any such claim at its own expense using the counsel of its own choosing, so long as [**] is in breach of any of its obligations under this Agreement. [**] will be responsible for [**]% of the amounts owed to any Third Party directly related to such claim, whether by settlement or judgment; and

(b) [**] in the Territory, [**] will have the right, but not the obligation, to defend any such claim at its own expense using the counsel of its own choosing. If [**]

exercises such right to defend, then it will be responsible for [**]% of the amounts owed to any Third Party directly related to such claim, whether by settlement or judgment.

In addition, with respect to any such claim by a Third Party that a Patent or other right controlled by such Third Party is infringed or will be infringed as a result of Licensee's activities under this Agreement in the Territory (whether or not [**]), the Parties will reasonably assist each other and cooperate and share information related to any such claim.

9.4.3 **Responsibility for Third Party Licenses**. If at any time during the Term, Akebia believes that it is necessary or advisable to seek to acquire or obtain a license from any Third Party in order to avoid infringement of Patents owned or controlled by such Third Party as a result of Licensee's activities under this Agreement, whether or not such Third Party has instituted an infringement claim, then Akebia will have the sole right, but not the obligation, [**] under such Patents from such Third Party. [**]. This Section 9.4.3 (Responsibility for Third Party Licenses) will not be interpreted as placing on either Party a duty of inquiry regarding Third Party intellectual property rights.

Article 10

MANUFACTURING AND SUPPLY

10.1. **Commercial Supply**. Subject to the terms and conditions of this Agreement and the Supply Agreement, Licensee will purchase from Akebia all of Licensee's requirements of the Licensed Products in Finished Form for sale in the Territory.

10.2. **Commercial Supply Agreement**. The Parties will use good faith efforts to negotiate and enter into a supply agreement for the commercial supply to Licensee of the Licensed Products in Finished Form (the "**Supply Agreement**") within [**] following the execution of this Agreement. The Supply Agreement will provide that, following acceptance by Akebia of a purchase order for Licensed Products, Akebia will invoice Licensee for the Transfer Price for such Licensed Products (as further described in Section 11.4 (Transfer Price)) at the time of delivery, payable within [**] following delivery.

Article 11

PAYMENTS

11.1. **Profit Share**. Subject to the provisions of this Agreement, as partial consideration for the License, Licensee will pay to Akebia 66.6% of the Profit accrued by Licensee or its Affiliates with respect to the sale of Licensed Products. Licensee will make such payment to Akebia in the manner described in Section 11.4 (Transfer Price).

11.2. **Upfront Payment**. Subject to the provisions of this Agreement, including Section 4.6 (Reimbursement System and Other Changes), as further consideration for the License, Licensee will pay to Akebia a non-creditable, nonrefundable payment of $25,000,000 (the "**Upfront Payment**") no later than [**] following the Effective Date.

11.3. **Equity Investment**. Licensee will purchase shares of common stock of Akebia for an aggregate purchase price of $20,000,000 at the purchase price and in accordance with the terms and conditions set forth in the Stock Purchase Agreement.

11.4. **Transfer Price**. Akebia will supply Licensed Products to Licensee under the Supply Agreement at a per-unit transfer price equal to [**] *plus* [**] *plus* [**] (the "**Transfer Price**"). At least [**] prior to the anticipated First Commercial Sale of the Licensed Product in the Territory, the Parties, through the Coordination Committee, will determine, for purposes of calculating the Transfer Price, the [**] for the calendar quarter following the First Commercial Sale. For each

subsequent calendar quarter, [**] will be determined based on the [**] in the most recently available calendar quarter, unless the Parties agree otherwise. Beginning from the First Commercial Sale, within [**] following the end of each calendar quarter, the Parties will reconcile the aggregate Transfer Price paid for Licensed Products against the [**] and [**] recorded in such calendar quarter. If Licensee has underpaid for such calendar quarter (*i.e.*, the aggregate Transfer Price paid is less than the sum of [**] *plus* [**] and [**] sold in such calendar quarter), then Licensee will make a true-up payment to Akebia in the amount of such underpayment. If Licensee has overpaid for such calendar quarter (*i.e.*, the aggregate Transfer Price paid is greater than the sum of [**] *plus* [**] and [**] sold in such calendar quarter), then Akebia will make a true-up payment to Licensee in the amount of such overpayment.

11.5. Working Capital Fund. Within [**] after the Effective Date, Licensee will pay Akebia $40,000,000 (the "**Initial Working Capital Payment**") to be used as a working capital fund to finance the manufacture of Licensed Products (the "**Working Capital Fund**"), representing [**]% of the amount of purchase orders that Akebia has placed with its contract manufacturer for the supply for the Territory of Licensed Product [**]. On a [**] basis, Akebia will notify Licensee of (a) all new purchase orders placed with Akebia's contract manufacturer in such [**] for Licensed Product scheduled to be delivered within the following [**], (b) following the Reimbursement Date, all purchase orders that have been fulfilled in the preceding [**], (c) the total amount of all outstanding purchase orders that Akebia has placed with its contract manufacturers as of the end of such [**], in each case, for the Territory (the "**Outstanding CMO Balance**"), (d) with respect to Akebia's inventory of Licensed Product drug substance, bulk drug product and finished goods as of the end of each [**] (the "**Safety Stock Amount**"), and (e) the sum of the Outstanding CMO Balance and the Safety Stock Amount ("**Total Working Capital Requirement**"), provided that, for the purpose of calculating the payments required by this Section 11.5 (Working Capital Fund), the Safety Stock Amount, when calculated as the number of months of forward coverage for the Territory, shall not exceed [**] for drug substance and [**] for the sum of bulk drug product and finished goods, unless the Parties explicitly agree to exceed such cap. Provided further, that such cap on the sum of bulk drug product and finished goods inventory shall not apply until [**] post Reimbursement Date. For clarity, nothing herein shall be construed as restricting the actual amount of Licensed Product inventory Akebia may maintain at any given time during the Term, or otherwise impacting Akebia's inventory management. Within [**] of receiving such notice, Licensee will contribute an additional amount (each such payment, an "**Additional Working Capital Payment**," and together with the Initial Working Capital Payment, the "**Working Capital Payments**"), to the Working Capital Fund, equal to the positive *difference* (if any) between (A) the Working Capital Percentage (defined below) *multiplied* by the Total Working Capital Requirement, *minus* (B) the current balance of the Working Capital Fund (*i.e.*, the total amount of all Working Capital Payments previously paid by Licensee to Akebia *minus* any refunds of such payments from Akebia to Licensee), provided that such Additional Working Capital Payment is greater than $[**], otherwise no additional contribution shall be due in that [**]. For clarity, if such difference is negative, then no payment from Licensee to Akebia shall be due. If, for a given [**], the Working Capital Fund exceeds the Working Capital Percentage *multiplied* by the Total Working Capital Requirement by an amount greater than $[**], then Akebia will refund to Licensee their entirety of such excess amount following such [**]. Upon any termination or expiration of this Agreement for any reason other than for convenience by Licensee pursuant to Section 16.9 (Termination by Licensee for Convenience), Akebia will refund to Licensee the then-outstanding balance of the Working Capital Fund, net of any amounts owed by Licensee to Akebia under the Agreement as of the effective date of such termination or expiration. The "Working Capital Percentage" will be [**]% as of the Effective Date, but the Coordination Committee will evaluate the Working Capital Percentage on a [**] basis during the Term, and will update it as appropriate to account for any substantial change in

the percentage of Licensee's share of overall purchase orders for Licensed Products for the Territory.

11.6. Sales Reports.

11.6.1 Monthly Reports.

(a) Within [**] after the end of each month in which Licensee or its Affiliates sell a Licensed Product to FMCNA, FMCNA's Affiliates, Majority Owned Clinics, or FKC Clinics, Licensee will provide to Akebia a report setting forth, (i) the number of units of Licensed Products sold by Licensee or its Affiliate to FMCNA, FMCNA's Affiliates, Majority Owned Clinics, or FKC Clinics, (ii) the actual gross sales of all Licensed Products sold by Licensee or its Affiliates to FMCNA, FMCNA's Affiliates, Majority Owned Clinics, or FKC Clinics in the Territory in such month; and (iii) the estimated total aggregate Net Sales of the Licensed Products sold by Licensee or its Affiliates to FMCNA, FMCNA's Affiliates, Majority Owned Clinics, or FKC Clinics in the Territory in such month.

(b) Within [**] after the end of each month in which Licensee or its Affiliate sells any Licensed Product to any Designated Wholesaler, Specialty Pharmacy or Authorized Dialysis Center (other than Majority Owned Clinics or FKC Clinics), Licensee will provide to Akebia a written report that sets forth: (i) the number of units of each Licensed Product supplied directly to any Designated Wholesaler, Specialty Pharmacy or Authorized Dialysis Center (other than Majority Owned Clinics or FKC Clinics), (ii) the gross sales for all Licensed Product supplied directly to any Designated Wholesaler, Specialty Pharmacy or Authorized Dialysis Center (other than Majority Owned Clinics or FKC Clinics), (iii) the Net Sales for all Licensed Product supplied directly to any Designated Wholesaler, Specialty Pharmacy or Authorized Dialysis Center (other than Majority Owned Clinics or FKC Clinics), (iv) the number of units of each Licensed Product held in inventory by any wholesaler, and (v) on a facility level, the number of units of each Licensed Product sold from Designated Wholesalers directly to Authorized Dialysis Centers (other than Majority Owned Clinics or FKC Clinics).

(c) Licensee will use Commercially Reasonable Efforts to negotiate the purchase of data from FMCNA, or relevant Specialty Pharmacy, in order to be able to report, on a facility level, the number of units of each Licensed Product distributed by FKC to FKC Clinics, or by Specialty Pharmacies to Authorized Dialysis Centers. Licensee shall confer with Akebia regarding terms of such agreement, prior to execution, and shall implement Akebia's reasonable comments with respect thereto. Akebia shall reimburse Licensee for [**]% of all documented costs associated with the purchase of such data, provided that Akebia has consented to the terms of such Agreement prior to its execution, provided further, that the Parties agree that Licensee's share of all documented costs associated with the purchase of such data shall not exceed [**] dollars ($[**]).

11.6.2 Quarterly Reports. In addition to the reports to be provided in accordance with Section 11.6.1 (Monthly Reports), (a) within [**] after the end of each calendar quarter in which Licensee or its Affiliate sells any Licensed Product, Licensee will provide to Akebia a written sales report that sets forth Net Sales of Licensed Products sold directly to FMCNA or any of its Affiliates including FKC, any Designated Wholesaler, each Specialty Pharmacy, each IDO, and each Third Party Dialysis Organization during such calendar quarter and the Profit in such calendar quarter from such sales, together with all calculations used to determine such Net Sales and Profit, and (b) within [**] after the end of each calendar quarter in which Licensee or its Affiliate sells any Licensed Product, Licensee will provide to Akebia a detailed written sales report (each, a "**Quarterly Report**") that sets forth (i) the units of each Licensed Product purchased directly by

FMCNA or any of its Affiliates including FKC, any Designated Wholesaler, any Specialty Pharmacy, the IDO members of each GPO, and each Third Party Dialysis Organization, and (ii) the number of units of each Licensed Product held in inventory by FMCNA or any of its Affiliates including FKC, each Specialty Pharmacy, each Designated Wholesaler, and any distributor of Licensee that distributes Licensed Products to IDOs or Third Party Dialysis Organizations, which, in each case ((i) and (ii)), will be broken down on a monthly and quarterly basis. In addition, on an annual basis, Licensee will provide to Akebia the annual Net Sales and Profit forecasts for each Licensed Product to be sold by Licensee under the License in the upcoming calendar year. The Parties will seek to resolve any questions or issues related to a Quarterly Report within [**] following receipt by Akebia of such Quarterly Report.

11.6.3 **Provisional Quarterly Reports**. Akebia may request Licensee to provide, within [**] after the end of each calendar quarter in which Licensee or its Affiliate sells any Licensed Product, a provisional report of the information described in Section 11.6.2 (Quarterly Reports), with the understanding that the information in such reports (each, a "**Provisional Quarterly Report**") is not official and will be subject to change.

11.7. **Accounting**. Licensee agrees to keep full, clear, and accurate records in accordance with the Accounting Standards consistently applied for a period of at least three years after the relevant payment is owed pursuant to this Agreement in sufficient detail to enable compensation payable to Akebia hereunder to be determined. Licensee further agrees to permit its books and records to be examined by an independent accounting firm selected by Akebia and approved by Licensee, which approval will not be unreasonably withheld or delayed, to verify the reports provided in Section 11.4 (Sales Reports). Such auditor will be bound by a legal agreement obligating it to maintain the confidentiality of such information and to not share it with Akebia. The auditor's report will be provided simultaneously to both Licensee and Akebia, will be limited to a disclosure of the extent of any underpayment or overpayment by Licensee in sufficient detail to allow Akebia and Licensee to understand the source of any error. Such audit will not be performed more frequently than once per calendar year. Such examination is to be made at the expense of Akebia, except in the event that the results of the audit reveal an underpayment by Licensee of [**]% or more during the period being audited, in which case reasonable audit fees for such examination will be paid by Licensee.

11.8. **Methods of Payment**. All payments due to Akebia under this Agreement will be made in U.S. Dollars by wire transfer to a bank account of Akebia designated from time-to-time in writing by Akebia.

11.9. **Late Payments**. Any amount owed by Licensee to Akebia under this Agreement that is not paid within the applicable time period set forth herein will accrue interest at the lesser of (a) the then current prime rate quoted by Citibank in New York City *plus* [**]%, or (b) the highest rate permitted under Applicable Law. If a Party disputes an invoice or other payment obligation under this Agreement, then such Party will timely pay the undisputed amount of the invoice or other payment obligation, and the Parties will resolve such dispute in accordance with Article 17 (Dispute Resolution; Governing Law).

Article 12

INFORMATION AND ADVERSE DRUG EVENTS AND REPORTS

12.1. **Data Security**. During the Term of this Agreement, Licensee will maintain and, as applicable, cause its Affiliates to maintain, environmental, safety, and facility procedures, data security procedures and other safeguards against the disclosure, destruction, loss, or alteration of any clinical data, post-marketing data, commercialization information, or any other information concerning the Licensed Compound or the Licensed Products known by Licensee or any of its Affiliates at any time during the Term that are no less rigorous than those maintained by Licensee (or any of its Affiliates) for its own information of a similar nature.

12.2. Adverse Drug Events. Licensee will provide to Akebia any information that it becomes aware of in the Territory concerning any adverse event relating to the Licensed Compound or any Licensed Product, whether or not determined to be attributable to the Licensed Compound or any Licensed Product, including any such information received by either Party from a Third Party (subject to receipt of any required consents from such Third Party) (such information, the "**Safety Data**") no later than [**] after becoming aware of any such Safety Data. Akebia will own all of the Safety Data, and the global safety database associated with the Licensed Products will be owned and maintained by Akebia. [**] will have the sole right and responsibility to administer and otherwise make decisions with respect to recalls and withdrawals of a Licensed Product, and [**] will, [**], provide assistance and cooperation reasonably requested by [**] in connection with any such recall or withdrawal.

Article 13

REPRESENTATIONS, WARRANTIES, AND COVENANTS

13.1. Mutual Representations and Warranties. Each of Licensee and Akebia hereby represents and warrants to the other Party as of the Effective Date that:

13.1.1 (a) It is a corporation or entity duly organized and validly existing under the laws of the state, municipality, provinces, administrative division, or other jurisdiction of its incorporation or formation, and (b) it has full power and authority and the legal right to own and operate property and assets and to carry on its business as it is now being conducted and as it is contemplated to be conducted by this Agreement.

13.1.2 The execution, delivery and performance of this Agreement by it has been duly authorized by all requisite corporate action.

13.1.3 This Agreement has been duly executed and delivered on behalf of such Party and constitutes a legal, valid, and binding obligation of such Party and is enforceable against such Party in accordance with its terms, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights and judicial principles affecting the availability of specific performance and general principles of equity.

13.1.4 It has the power and authority to execute and deliver this Agreement and to perform its obligations hereunder, and such performance does not conflict with or constitute a breach of any of its agreements with Third Parties.

13.1.5 It has obtained all necessary consents, approvals, and authorizations of all Governmental Authorities and other Third Parties required to be obtained in connection with the execution and delivery of this Agreement and the performance of its obligations hereunder.

13.1.6 The execution and delivery of this Agreement and the performance of its obligations hereunder (a) do not conflict with or violate any requirement of Applicable Law or any provision of its articles of incorporation, bylaws, limited partnership agreement, or any similar instrument, as applicable, and (b) do not conflict with, violate, or breach or constitute a default or require any consent under, any Applicable Law or any contractual obligation or court or administrative order by which it is bound.

13.1.7 It has the right to grant the rights and licenses described in this Agreement.

13.2. Additional Mutual Representations and Warranties. Each of Licensee and Akebia represents and warrants as of the Effective Date that it has not been debarred by the FDA, is not the subject of a conviction described in Section 306 of the FD&C Act, and is not subject to any similar sanction of other Governmental Authorities outside of the Territory, and neither it nor any of its Affiliates has used, in any capacity, any person who either has been debarred by the FDA, is the

subject of a conviction described in Section 306 of the FD&C Act, or is subject to any such similar sanction.

13.3. Additional Akebia Representations and Warranties. Akebia hereby represents and warrants as of the Effective Date that:

13.3.1 The Akebia Patents and the Akebia Trademarks have been duly filed in the Territory.

13.3.2 All applicable filing, maintenance, and other fees have been timely paid for all of the Akebia Patents set forth on Schedule 1.9 and the Akebia Trademarks set forth on Schedule 1.11, and, to Akebia's Knowledge, all of the Akebia Patents set forth on Schedule 1.9 that are issued patents and the Akebia Trademarks set forth on Schedule 1.11 that are registered trademarks, in each case, are in full force and effect.

13.3.3 There is no pending or, to Akebia's Knowledge, threatened (in writing) re-examination, opposition, interference, *inter partes* review, or claim challenging the inventorship, ownership, validity, enforceability, or patentability of the Akebia Patents or other litigation or proceeding in the Territory relating to any of the Akebia Patents.

13.3.4 The sale of the Licensed Products does not and will not infringe any valid Patent or other intellectual property rights of any Third Party in the Territory.

13.3.5 Akebia has received no written notice of any claim that a patent or trade secret owned or controlled by a Third Party is or would be infringed or misappropriated by the sale of the Licensed Products in the Territory.

13.3.6 To Akebia's Knowledge, there is no use, infringement, or misappropriation of the Akebia Technology in the Territory in derogation of the rights granted to Licensee in this Agreement.

13.3.7 There are no investigations, inquiries, actions, or other proceedings pending before or to Akebia's Knowledge threatened by the FDA or other Governmental Authority in the Territory with respect to the Licensed Products arising from any default by Akebia or a Third Party acting on behalf Akebia in the research or development of the Licensed Compound, and Akebia has not received written notice threatening any such investigation, inquiry, action or other proceeding.

13.3.8 Akebia owns or has licensed the rights, title, and interests in and to the Akebia Technology granted to Licensee pursuant the License.

13.3.9 The research, development, and manufacture of the Licensed Products conducted by Akebia or its Affiliates has been conducted in compliance with Applicable Law and, to Akebia's Knowledge, the research, development, and manufacture of the Licensed Products conducted by Akebia's Third Party contractors has been conducted in compliance with Applicable Law.

13.4. Additional Licensee Representations and Warranties. Licensee hereby represents and warrants as of the Effective Date that:

13.4.1 Vifor Pharma Participations Ltd. and Fresenius Medical Care AG & Co KGaA are the joint venture partners of VFMCRP, with Vifor Pharma Participations Ltd. owning a controlling interest of VFMCRP and Fresenius Medical Care AG & Co KGaA owning the remaining interest.

13.4.2 FKC is an Affiliate of FMCNA and a strategic partner of Licensee.

13.4.3 FreseniusRx is an Affiliate of FMCNA.

13.4.4 Licensee is not an Affiliate of FMC, FMCNA or any member of the Licensee Supply Group.

13.4.5 Licensee is a drug manufacturer that is not engaged in the wholesale distribution of prescription drugs to "retail community pharmacies" (as that term is defined in 42 U.S.C. § 1396r-8(k)(10)).

13.4.6 The transmission of all information required to be included in each Quarterly Report and Monthly Reports pursuant to this Agreement is consistent with Applicable Law and Licensee's contractual obligations with Third Parties.

13.5. Additional Covenants.

13.5.1 Each Party covenants that it will not engage, in any capacity in connection with this Agreement or any ancillary agreements, any person who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act, or is subject to any such similar sanction. Each Party will inform the other Party in writing promptly if it or any person engaged by it or any of its Affiliates who is performing services under this Agreement, or any ancillary agreements, is debarred or is the subject of a conviction described in Section 306 of the FD&C Act, or if any action, suit, claim, investigation, or legal or administrative proceeding is pending or, to each Party's knowledge, is threatened, relating to the debarment or conviction of a Party, any of its Affiliates, or any such person performing services hereunder or thereunder.

13.5.2 Each Party covenants that it will comply with all Applicable Laws in performing its activities hereunder.

13.5.3 If either Party determines, based on reasonable advice of counsel, that its compliance with this Agreement will violate Applicable Law, then the Parties will negotiate to amend this Agreement as necessary to ensure that the terms hereof to permit such Party to comply with Applicable Law and this Agreement during the Term.

13.5.4 Licensee covenants that throughout the Term it will not, and will cause each of its Affiliates that are involved in the supply or distribution of any Licensed Product to not, engage in the wholesale distribution of prescription drugs to "retail community pharmacies" (as that term is defined in 42 U.S.C. § 1396r-8(k)(10)) in the Territory.

13.5.5 Licensee covenants that throughout the Term it will provide prompt written notice to Akebia in the event that any of its Affiliates intends to engage, or has engaged, in the wholesale distribution of prescription drugs to "retail community pharmacies" (as that term is defined in 42 U.S.C. § 1396r-8(k)(10)) in the Territory.

13.5.6 Licensee covenants that, throughout the term, Licensee will not provide to FreseniusRx any preferential discounts or rebates that Licensee does not also make available to all other Specialty Pharmacies.

13.5.7 Neither Party will enter into any agreement or contractual obligation with a Third Party that conflicts with or is inconsistent with this Agreement or requires the consent of any Third Party for such Party to perform its obligations under this Agreement.

13.5.8 On the Effective Date, Akebia will provide to Licensee an updated Schedule 1.9 that includes all Akebia Patents as of the Effective Date, and an updated Schedule 1.11 that includes all Akebia Trademarks as of the Effective Date.

13.6. Disclaimer. EXCEPT AS EXPRESSLY SET FORTH HEREIN, INCLUDING THE WARRANTIES SET FORTH IN SECTION 13.3 (ADDITIONAL AKEBIA REPRESENTATIONS AND WARRANTIES), THE INTELLECTUAL PROPERTY RIGHTS

PROVIDED BY AKEBIA ARE PROVIDED "AS IS" AND WITHOUT WARRANTY. EXCEPT AS EXPRESSLY SET FORTH HEREIN, INCLUDING THE WARRANTIES SET FORTH IN SECTION 13.3 (ADDITIONAL AKEBIA REPRESENTATIONS AND WARRANTIES), AKEBIA EXPRESSLY DISCLAIMS ANY AND ALL WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING THE WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY, OR ENFORCEABILITY OF ITS RESPECTIVE INTELLECTUAL PROPERTY RIGHTS, AND NONINFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES, ARISING FROM A COURSE OF DEALING, USAGE, OR TRADE PRACTICES, IN ALL CASES WITH RESPECT THERETO.

13.7. **Limitation of Liability**. NEITHER OF THE PARTIES WILL BE ENTITLED TO RECOVER FROM THE OTHER PARTY ANY SPECIAL, INCIDENTAL, INDIRECT, CONSEQUENTIAL, OR PUNITIVE DAMAGES OR DAMAGES FOR LOSS OF PROFIT OR LOST OPPORTUNITY IN CONNECTION WITH THIS AGREEMENT, ITS PERFORMANCE OR LACK OF PERFORMANCE HEREUNDER, OR ANY LICENSE GRANTED HEREUNDER, EXCEPT TO THE EXTENT THE DAMAGES RESULT FROM A PARTY'S WILLFUL MISCONDUCT, OR INTENTIONAL BREACH OF ITS OBLIGATIONS UNDER THIS AGREEMENT, A BREACH OF THE OBLIGATIONS OF A PARTY UNDER [**], A VIOLATION BY A PARTY OR ITS AFFILIATES OF [**].

Article 14

CONFIDENTIALITY

14.1. **Generally**. During the Term and for a period of seven years following the early termination of this Agreement, each Party (a) will maintain in confidence all Confidential Information of the other Party; (b) will not use such Confidential Information for any purpose except in connection with the activities contemplated by this Agreement or in order to further the purpose of this Agreement; and (c) will not disclose such Confidential Information, except that each Party may disclose such Confidential Information to its Affiliates, investors, prospective investors, lenders, prospective lenders, financing sources, prospective financing sources (including, in each case, in connection with any royalty factoring or similar transaction), prospective acquirers, licensees, sublicensees, prospective sublicensees, employees, consultants, financial or legal advisors, agents, or subcontractors who are bound by obligations of nondisclosure and non-use no less stringent than those set forth in this Article 14 (Confidentiality) and to whom such disclosure is reasonably necessary or advisable in connection with such Party's activities as contemplated in this Agreement or in connection with financing or acquisition activities (including its right to assign its rights hereunder pursuant to Section 18.1 (Assignment) as part of a royalty factoring or other similar transaction). Each Party will ensure that its Affiliates, investors, prospective investors, lenders, prospective lenders, acquirors, licensees, sublicensees, prospective acquirors, licensees, sublicensees, prospective sublicensees, employees, consultants, agents, consultants, and subcontractors comply with these obligations. Each Party will notify the other Party promptly on discovery of any unauthorized use or disclosure of the other Party's Confidential Information, including the other Party's trade secrets or proprietary information. Licensee acknowledges that all (i) Safety Data, (ii) Akebia Know-How, and (iii) other information related to Akebia's and its Affiliates', licensees', and sublicensees' development and commercialization of the Licensed Compound and the Licensed Products constitutes Confidential Information of Akebia. The terms of this Agreement will be the Confidential Information of each Party.

14.2. **Exceptions**. The obligations of confidentiality, non-disclosure, and non-use set forth in Section 14.1 (Generally) will not apply to the extent the receiving Party (the "**Recipient**") can demonstrate that the disclosed information (a) was in the public domain at the time of disclosure to the Recipient by the other Party, or thereafter entered the public domain, in each case, other than as a result of actions of the Recipient, its Affiliates, employees, licensees, agents, or subcontractors, in breach of this Agreement; (b) was rightfully known by the Recipient or its Affiliates (as shown by its written records) prior to the date of disclosure to the Recipient by the other Party; (c) was received by the Recipient or its Affiliates on an unrestricted basis from a

Third Party rightfully in possession of such information and not under a duty of confidentiality to the other Party; or (d) was independently developed by or for the Recipient or its Affiliates without reference to or reliance on the Confidential Information of the other Party (as demonstrated by written records). Notwithstanding any other provision of this Agreement, the Recipient's disclosure of Confidential Information will not be prohibited if such disclosure: (i) is in response to a valid order of a court or other Governmental Authority; or (ii) is otherwise required by Applicable Law or regulation or rules of a nationally recognized securities exchange. Further notwithstanding any other provision of this Agreement, Akebia may disclose Licensee's Confidential Information to the extent disclosure is required in connection with the filing or prosecuting patent applications, prosecuting, or defending litigation, responding to an investigation by a Governmental Authority, or otherwise establishing rights or enforcing obligations under this Agreement, making Regulatory Filings with respect to the Licensed Products, or conducting research, development, or clinical studies with respect to the Licensed Products. If a Recipient is required to disclose Confidential Information pursuant to this Section 14.2 (Exceptions), then prior to any disclosure the Recipient will provide the other Party with prior written notice of such disclosure in order to permit the other Party to seek a protective order or other confidential treatment of such Confidential Information.

14.3. **Publicity**. The Parties recognize that each Party may from time-to-time desire to issue press releases and make other public statements or disclosures regarding the terms of this Agreement. In such event, the Party desiring to issue a press release or make a public statement or disclosure will provide the other Party with a copy of the proposed press release, statement, or disclosure for review and approval as soon as practicable prior to publication, which advance approval will not be unreasonably withheld or delayed. No other public statement or disclosure of, or concerning, the terms of this Agreement will be made, either directly or indirectly, by either Party, without first obtaining the written approval of the other Party. Once any public statement or disclosure has been approved in accordance with this Section 14.3 (Publicity), then either Party may appropriately communicate information contained in such permitted statement or disclosure. Notwithstanding the foregoing provisions of this Article 14 (Confidentiality), a Party may disclose the terms of this Agreement where required, as reasonably determined by the disclosing Party, by Applicable Law, regulation or legal process, or by applicable stock exchange rule (with prompt notice of any such legally required disclosure to the other Party and, to the extent practicable, sufficient opportunity for the other Party to review and comment on such required disclosure and request confidential treatment thereof or a protective order therefor).

14.4. **Publications**. If, [**], Licensee, its Affiliates, FMCNA, the Licensee Supply Group, or any healthcare professional having an investigator initiated trial agreement in place with any of the previously listed entities desires to publish any clinical data or other clinic results from the administration of the Licensed Compound or any Licensed Product, then Licensee will, will cause its Affiliates to, and will cause FMCNA, the Licensee Supply Group, and such healthcare professionals to, in each case, [**]. If Akebia determines that any such proposed publication contains patentable subject matter requiring protection, then Akebia may require the delay of such publication for a period of time not to exceed an additional [**] to pursue such protection or negotiate with such healthcare professional. If Akebia determines that the proposed publication contains Confidential Information, then Akebia may require such Confidential Information to be deleted from such publication. If, [**], Licensee, its Affiliates, FMCNA, or the Licensee Supply Group desires to publish any preclinical or non-clinical results from the research and development of the Licensed Compound or any Licensed Product, then Licensee will, will cause its Affiliates to, and will cause FMCNA and the Licensee Supply Group to, in each case, [**].

Article 15

INDEMNIFICATION

15.1. **Indemnification by Akebia**. Unless otherwise provided herein, Akebia will indemnify, hold harmless, and defend Licensee and its Affiliates and their respective, directors, officers, employees, and agents (the "**Licensee Indemnitees**") from and against any and all Third Party suits, claims, actions, demands, liabilities, expenses, or losses (including reasonable attorneys'

fees, court costs, witness fees, damages, judgments, fines, and amounts paid in settlement) ("**Losses**") to the extent that such Losses arise out of (a) a breach of this Agreement by Akebia, (b) [**] of a Licensed Product by or on behalf of Akebia or its Affiliates or licensees (other than Licensee, the LSP, Designated Wholesalers, or a member of the Licensee Supply Group), or (c) the negligence or willful misconduct of any Akebia Indemnitee (as defined in Section 15.2 (Indemnification by Licensee)). Notwithstanding the foregoing, Akebia will not have any obligation to indemnify the Licensee Indemnitees to the extent that any Losses arise out of the negligence or willful misconduct of any Licensee Indemnitee or any breach of this Agreement by Licensee.

15.2. Indemnification by Licensee. Unless otherwise provided herein, Licensee will indemnify, hold harmless, and defend Akebia and its Affiliates and their respective directors, officers, employees, and agents (the "**Akebia Indemnitees**") from and against any and all Losses, to the extent that such Losses arise out of (a) a breach of this Agreement by Licensee, (b) [**], in each case, of a Licensed Product by or on behalf of Licensee, the LSP, Designated Wholesalers, or the Licensee Supply Group (including any communications regarding such Licensed Product by Licensee, the LSP, or the Licensee Supply Group), or (c) the negligence or willful misconduct of any Licensee Indemnitee. Notwithstanding the foregoing, Licensee will not have any obligation to indemnify the Akebia Indemnitees (i) to the extent that any Losses arise out of the negligence or willful misconduct of any Akebia Indemnitee or any breach of this Agreement by Akebia, or (ii) for any [**] of any Licensed Product, other than any [**] of any Licensed Product by or on behalf of Licensee, the LSP, Designated Wholesalers, or the Licensee Supply Group.

15.3. Indemnification Procedure. Each Party, if seeking indemnification under this Article 15 (Indemnification) (the "**Indemnified Party**"), will give [**] written notice of the claim to the other Party (the "**Indemnifying Party**"); *provided*, *however*, that any failure or delay in providing such notice will not relieve the Indemnifying Party of its indemnification obligation, except to the extent it is actually prejudiced by such failure or delay. Each Party will promptly furnish to the other Party copies of all papers and official documents received in respect of any Losses. The Indemnifying Party will have the right, exercisable by written notice to the Indemnified Party, to assume and control the defense of the indemnification claim at its own expense with counsel selected by the Indemnifying Party and reasonably acceptable to the Indemnified Party; *provided*, *however*, that an Indemnified Party will have the right to retain its own counsel, at its own expense, except that the fees and expenses of the Indemnified Party's counsel will be paid by the Indemnifying Party if representation of such Indemnified Party by the counsel retained by the Indemnifying Party would be inappropriate due to actual or potential differing interests between the Indemnified Party and any other party represented by such counsel in such proceedings. If the Indemnifying Party does not assume the defense of the indemnification claim as described in this Section 15.3 (Indemnification Procedure), then the Indemnified Party may defend the indemnification claim but will have no obligation to do so. The Indemnified Party will not settle or compromise the indemnification claim without the prior written consent of the Indemnifying Party, and the Indemnifying Party will not settle or compromise the indemnification claim in any manner that would have an adverse effect on the Indemnified Party's interests (including any rights under this Agreement or the scope or enforceability of any Patents, Confidential Information, or other rights licensed to Licensee by Akebia hereunder), without the prior written consent of the Indemnified Party, which consent, in each case (by the Indemnifying Party or Indemnified Party, as the case may be), will not be unreasonably withheld or delayed. The Indemnified Party will reasonably cooperate with the Indemnifying Party at the Indemnifying Party's expense and will make available to the Indemnifying Party all pertinent information under the control of the Indemnified Party, which information will be subject to Article 14 (Confidentiality). The Indemnifying Party will provide periodic updates to the Indemnified Party (and its counsel, if applicable) regarding its defense of the action with immediate notice regarding any material developments. The Indemnifying Party will not be liable for any settlement or other disposition of Losses by the Indemnified Party if such settlement is reached without the written consent of the Indemnifying Party pursuant to this Section 15.3 (Indemnification Procedure).

15.4. **Reimbursement of Additional Expenses**. Notwithstanding any provision to the contrary set forth in this Agreement, Licensee will reimburse Akebia for all reasonable actual out-of-pocket expenses (including, but not limited to, attorneys' fees and costs, and all other expenses) incurred by Akebia in connection with responses to subpoenas, government investigations and other similar legal orders and legal and regulatory processes issued to Akebia with respect to Licensee or any of its Affiliates or Designated Wholesalers, the Licensee Supply Group, or the subject matter of this Agreement. Licensee, however, shall have no obligation to reimburse Akebia for any such expenses directly arising out of, in connection with or otherwise relating to actions or omissions of Akebia or its employees, officers, directors or Affiliates that violate this Agreement or Applicable Law.

15.5. **Insurance**. Akebia and Licensee will each, at their own expense, obtain and maintain insurance with respect to the use and sale of the Licensed Products under this Agreement in such amount and subject to such deductibles and other limitations as biopharmaceutical companies in the Territory customarily maintain with respect to the use and sale of similar products. Each Party will provide a copy of such insurance policy to the other Party upon request.

Article 16

TERM AND TERMINATION

16.1. **Term**. The term of this Agreement will begin on the Original Execution Date and, unless earlier terminated in accordance with the terms of this Article 16 (Term and Termination), will extend until the later of (a) expiration of the last-to-expire Valid Claim [**] that would, but for the licenses granted hereunder, be infringed by the making, using, selling, or importing of such Licensed Product in the Territory, or (b) expiration of marketing or regulatory exclusivity in the Territory (the "**Term**").

16.2. **Termination for Breach**. Subject to the terms and conditions of this Section 16.2 (Termination for Breach), a Party (the "**Non-Breaching Party**") will have the right, in addition to any other rights and remedies, to terminate this Agreement in its entirety in the event the other Party (the "**Breaching Party**") is in material breach of any of its obligations under this Agreement. The Non-Breaching Party will first provide written notice to the Breaching Party, which notice will identify with particularity the alleged breach and state the Non-Breaching Party's intent to terminate this Agreement if such breach is not cured. With respect to material breaches of any payment provision hereunder, the Breaching Party will have a period of [**] after such written notice is provided to cure such breach. With respect to all other breaches, the Breaching Party will have a period of [**] after the Non-Breaching Party provides written notice to cure such breach. Notwithstanding the foregoing, if a Non-Breaching Party provides notice to the Breaching Party pursuant to this Section 16.2 (Termination for Breach) of an alleged material breach by such Breaching Party, and such Non-Breaching Party provides notice during the applicable cure period set forth above that such Non-Breaching Party disputes the basis for termination pursuant to this Section 16.2 (Termination for Breach) and initiates the dispute resolution procedure set forth in Article 17 (Dispute Resolution; Governing Law) during the applicable cure period, then the cure periods set forth in this Section 16.2 (Termination for Breach) for the alleged material breach will run from the date that such written notice is first provided to the Breaching Party through the resolution of such dispute pursuant to Article 17 (Dispute Resolution; Governing Law) and it is understood and acknowledged that, during the pendency of a dispute pursuant this Section 16.2 (Termination for Breach), all of the terms and conditions of this Agreement will remain in effect, and the Parties will continue to perform all of their respective obligations under this Agreement. The waiver by either Party of any breach of any term or condition of this Agreement will not be deemed a waiver as to any subsequent or similar breach.

16.3. **Termination for Bankruptcy**. Subject to the terms and conditions of this Agreement, either Party may terminate this Agreement upon notice to the other Party should the other Party: (a) consent to the appointment of a receiver or a general assignment for the benefit of creditors of the other Party that is not discharged within [**], or (b) file a petition under any bankruptcy or

insolvency law or have any such petition filed against it that has not been stayed within [**] of such filing.

16.4. Termination by Akebia for Unauthorized Sales.

16.4.1 Termination of the Agreement for Unauthorized Sales. If the Parties do not reach a resolution of a matter under discussion pursuant to Section 4.1 (No Unauthorized Sales) during the [**] period for the Parties to reach a resolution as set forth therein, or Licensee does not (a) [**] any unauthorized use, distribution, or transfer of the Licensed Compound or any Licensed Product by Licensee, FKC, any Specialty Pharmacy, the LSP, a TPDO, any Authorized Dialysis Center, any Designated Wholesaler, or any distributor associated with any of the foregoing, or (b) [**] of Licensed Products to FKC, Specialty Pharmacy, LSP, TPDO, Authorized Dialysis Center, or Designated Wholesaler that is using, distributing, or transferring the Licensed Compound or any Licensed Product other than as expressly permitted under this Agreement, then, in each case ((a) and (b)), Akebia may terminate this Agreement with immediate effect upon written notice to Licensee.

16.4.2 Termination of GPO or IDO for Unauthorized Sales. Notwithstanding Section 16.4.1 (Termination of the Agreement for Unauthorized Sales), if the applicable matter under discussion pursuant to Section 4.1 (No Unauthorized Sales) relates to any unauthorized use, distribution, or transfer of any Licensed Product by any distributor used by a GPO, IDO, or IDO Clinic, and the Parties do not reach a resolution of the applicable matter during the [**] period for the Parties to reach a resolution as set forth under Section 4.1 (No Unauthorized Sales), or Licensee does not (a) [**] such unauthorized use, distribution, or transfer of the Licensed Compound or any Licensed Product by such distributor used by a GPO, IDO, IDO Clinic, as applicable, or (b) Licensee does not [**] of Licensed Product to such distributor used by a GPO, IDO, IDO Clinic, as applicable, then Akebia may, in its sole discretion and without limiting its rights set forth in Section 16.4.1 (Termination of the Agreement for Unauthorized Sales), elect to either (i) [**] to sell the Licensed Products, indirectly through a distributor, to such GPO's IDO members with immediate effect upon written notice to Licensee, in which case Licensee will immediately stop supplying Licensed Products, directly or indirectly through a distributor, to such GPO's IDO members and terminate the Licensee-GPO Supplier Agreement or (ii) in the case of any unauthorized use, distribution, or transfer of any Licensed Product by any IDO, [**], in which case Licensee will cause the applicable GPO and any distributor that supplies such GPO to (x) [**] of Licensed Products to such IDO and (y) cause such GPO to [**] such IDO's right to purchase Licensed Products with immediate effect upon written notice to Licensee.

16.5. Termination by Akebia Upon Occurrence of Certain Events. If any of the following events occur, then Akebia may terminate this Agreement with immediate effect upon written notice to Licensee:

16.5.1 Licensee or its Affiliate involved in the supply or distribution of any Licensed Product becomes an Affiliate of FMC, FMCNA or any member of the Licensee Supply Group; or

16.5.2 There is no affiliation or other strategic relationship between Licensee or its Affiliate involved in the supply or distribution of any Licensed Product and FMC or FMCNA.

16.6. Termination by Akebia for Failure to Enter Into or Amend the Licensee-FKC Supply Agreement or Licensee-FreseniusRx Supply Agreement. Akebia may terminate this Agreement with immediate effect upon written notice to Licensee if (a) Licensee (either directly or indirectly through VFMCRP) does not enter into an amendment of the Licensee-FKC Supply Agreement in accordance with Section 5.1.2 (Amendment to Supply Agreement) within [**] after the Reimbursement Date, (b) in the event the Licensee-FKC Supply Agreement does not include sales to FreseniusRx, Licensee (either directly or indirectly through VFMCRP) does not enter into

the Licensee-FreseniusRx Supply Agreement, or an amendment thereto, in accordance with Section 5.3 (Licensee-FreseniusRx Supply Agreement) within [**] after the Reimbursement Date, or (c) the Licensee-FKC Supply Agreement or Licensee-FreseniusRx Supply Agreement is terminated or expires, *unless*, solely as it relates to termination of the Licensee-FreseniusRx Supply Agreement, the Parties agree in writing to the termination of such agreement in accordance with Section 5.3.

16.7. Termination or Suspension by Akebia for Impacts on Pricing. If, at any time, (a) there has been a breach of Section 6.1 (Pricing) or Section 6.4 (No Effect on Licensed Product Reported Pricing), (b) through the actions by or on behalf of Licensee, any of its Affiliates, any Designated Wholesaler, or any member of the Licensee Supply Group (even if pursuant to Licensee Supply Group's customary dialysis clinic cost reporting to CMS or any other Governmental Authority, and even if such actions do not constitute a breach by Licensee under Section 4.4 (Licensed Product Prices)), any Third Party purchaser or potential purchaser (other than either Party's Affiliates or FMCNA, FMCNA's Affiliates (including FKC and FreseniusRx), or Majority Owned Clinics) becomes aware of the price at which Licensee, any of its Affiliates, any Designated Wholesaler, or any member of the Licensee Supply Group acquired any Licensed Product, or the price at which such entity sells any Licensed Product to any purchaser (even if pursuant to Licensee Supply Group's customary dialysis clinic cost reporting to CMS or any other Governmental Authority), (c) [**], or (d) Licensee or any of its Affiliates sells, or plans to sell, any Licensed Product in any manner that [**], and, in each case ((a) through (d)), the Parties do not reach an agreeable resolution within [**] after Akebia notifies Licensee of its intent to terminate based on such condition, then, in either case, Akebia may elect to either (i) terminate this Agreement or (ii) suspend the License and commence a Suspension Period under Section 3.2.2 (Suspension), in each case ((i) and (ii)), with immediate effect upon written notice to Licensee. If Akebia elects to suspend the License, Akebia may reinstate the License (such reinstatement resuming the Effective Period) at any time during the Term upon written notice to Licensee.

16.8. Termination by Akebia for Patent Challenge. Akebia may terminate this Agreement with immediate effect upon written notice to Licensee if Licensee or any of its Affiliates contests the validity or enforceability of any Patent Controlled by Akebia or any of its Affiliates that Covers a Licensed Product or its manufacture, use, sale, or importation, in any court, arbitration proceeding, or other tribunal, including the United States Patent and Trademark Office and the United States International Trade Commission. As used in this definition, the term "contest" includes (a) filing an action under 28 U.S.C. §§ 2201-2202 seeking a declaration of invalidity or unenforceability of any such Patent; (b) filing, or joining in, a petition under 35 U.S.C. § 311 to institute *inter partes* review of any such Patent; (c) filing, or joining in, a petition under 35 U.S.C. § 321 to institute post-grant review of any such Patent or any portion thereof; (d) filing or commencing any opposition, nullity, or similar proceedings challenging the validity of any such Patent in any country, or (e) any foreign equivalent of clauses (a), (b), (c), or (d).

16.9. Termination by Licensee for Convenience. At any time after the first anniversary of the receipt of Regulatory Approval for the Licensed Product in the DD-CKD Indication, Licensee may terminate this Agreement in its entirety by providing written notice to Akebia thereof, which termination will be effective 30 months following the date of such notice; *provided*, *however*, that (a) such 30-month notice period may be shortened by written agreement of both Akebia and Licensee and (b) in the event that the FDA issues a Complete Response Letter in response to the NDA for the Licensed Product, then Licensee may terminate this Agreement at any time within 30 days of receiving notice of such Complete Response Letter from Akebia by providing written notice of termination to Akebia, which termination will be effective 30 days after Licensee provides such termination notice to Akebia, *provided* that in such event any payments required to be made to Akebia prior to the effective date of such termination will continue to be due and upon receipt by Akebia will be non-refundable and non-creditable.

16.10. Termination by Akebia for Convenience. Akebia may terminate this Agreement in its entirety for convenience at any time following the earlier of (a) 18 months following the later of (i) the

Reimbursement Date and (ii) the date of the topline data readout of the TIW Modify Trial or (b) the second anniversary of the receipt of Regulatory Approval for the Licensed Product from the FDA. Any such termination by Akebia in accordance with this Section 16.10 (Termination by Akebia for Convenience) will be effective six months after the date on which Akebia provides written notice of such termination to Licensee.

16.10.1 Termination Fee. If Akebia terminates this Agreement in accordance with Section 16.10 (Termination by Akebia for Convenience), then Akebia will pay to Licensee a termination fee based on the volume of Licensed Product sold by Licensee prior to the date of such termination and the profit generated by Akebia following the date of such termination. Within [**] following each calendar quarter during the Tail Period, Akebia will pay to Licensee a fee equal to [**] (such payments, collectively, the "**Termination Fee**"). For purposes of the Termination Fee:

"**Licensee's Pre-Termination Average Sales Volume**" means: [**]. Notwithstanding the foregoing, if Akebia materially breaches the Supply Agreement during the [**] period prior to that date of Akebia's notice of such termination, and such material breach results in a material disruption in the supply of Licensed Products to Licensee, then Licensee's Pre-Termination Average Sales Volume will be calculated [**].

"**Tail Period**" means the [**] period following the effective date of such termination.

"**Licensee's Tail Period Profit Share**" means, for a given calendar quarter during the Tail Period, an amount equal to [**]% of Akebia's average per-unit Profit during such calendar quarter, with Akebia calculating its per-unit Profit *mutatis mutandis* in the same manner that Licensee did prior to such termination.

16.10.2 Commercialization of Competing Product. If Akebia terminates this Agreement pursuant to Section 16.10 (Termination by Akebia for Convenience), then Licensee may Promote, sell or have sold a Competing Product in the Field in the Territory at any time after the date of termination of this Agreement. If Licensee or any of its Affiliates Promotes, sells or has sold a Competing Product in the Field in the Territory at any time during the Tail Period, then Akebia will have no further obligation to pay any amount of the Termination Fee yet unpaid as of the date Licensee commences Promoting, selling, or having sold a Competing Product in the Territory.

16.11. Termination Following Bundle Exclusion. If CMS determines that the Licensed Product is excluded from the ESRD PPS Bundled Payment System and TDAPA, then, during the [**] period after Akebia is notified of such determination by CMS, Akebia may terminate this Agreement effective upon not less than [**] prior written notice to Licensee. If Akebia terminates this Agreement in accordance with this Section 16.11 (Termination Following Bundle Exclusion), then Akebia will (a) repay the Upfront Payment to Licensee, (b) pay an amount equal to [**] (as defined in the Stock Purchase Agreement) (*i.e.*, the per-share premium above the trading average of the market value of such shares as of the Closing Date (as defined in the Stock Purchase Agreement) *multiplied* by number of shares acquired by Licensee), and (c) pay Licensee [**].

16.12. Termination Based on Written Agreement of the Parties. This Agreement may be terminated in its entirety upon the written agreement of both Akebia and Licensee.

16.13. Effects of Termination. In the event of any expiration or termination of this Agreement in its entirety, the following will apply:

16.13.1 Termination of Licenses. Except as expressly set forth in this Section 16.13 (Effects of Termination), and subject to Section 16.16 (Survival; Accrued Rights), all rights and licenses granted to Licensee under this Agreement will automatically terminate.

16.13.2 Return of Confidential Information. Licensee will cease using the Akebia Technology and will return to Akebia all copies of any documents containing any Akebia Know-How. Each Party will return or destroy all Confidential Information of the other Party in its possession upon expiration or termination of this Agreement at the disclosing Party's election and written request. The Recipient will provide a written confirmation of such destruction within [**] of such request; *provided*, *however*, that the foregoing will not apply to any Confidential Information that is necessary to allow such Party to perform its obligations or exercise any of its rights that expressly survive the termination or expiration of this Agreement, *provided*, *further*, that [**].

16.13.3 Cessation of Sales. Except for sales made in accordance with Section 16.13.4(a)(i) (Termination Other than for Cause by Akebia), Licensee will cease all sales of Licensed Product in the Territory.

16.13.4 Sell-Off or Buy-Back.

(a) Termination Other than for Cause by Akebia. If this Agreement is terminated by Licensee pursuant to Section 16.3 (Termination for Bankruptcy), Section 16.10 (Termination by Akebia for Convenience), or Section 16.11 (Termination Following Bundle Exclusion) then, after the effective date of such termination: (i) Licensee may continue to sell the Licensed Products for a period of [**] after the effective date of such termination in order to fill existing binding orders and commitments, and (ii) following such [**] period, at Akebia's option and in its sole discretion, [**] for such Licensed Products by Licensee or its Affiliates. Licensee will destroy, or cause to be destroyed, all Licensed Products remaining in inventory that [**] following such [**] period, at Licensee's cost and expense.

(b) Termination for Cause by Akebia. If this Agreement is terminated by Akebia pursuant to Section 16.2 (Termination for Breach), Section 16.4.1 (Termination of the Agreement for Unauthorized Sales), Section 16.5 (Termination by Akebia Upon Occurrence of Certain Events), Section 16.6 (Termination by Akebia for Failure to Enter Into or Amend the Licensee-FKC Supply Agreement or Licensee-FreseniusRx Supply Agreement), Section 16.7 (Termination or Suspension by Akebia for Impacts on Pricing), or Section 16.8 (Termination by Akebia for Patent Challenge), then, after the effective date of such termination, at Akebia's option in its sole discretion, [**] for such Licensed Products by Licensee or its Affiliates. Licensee will destroy, or cause to be destroyed, all Licensed Products remaining in inventory as of the effective date of termination that [**], at Licensee's cost and expense.

16.14. Effects of Termination With Respect to GPO or TPDO. If this Agreement is terminated with respect to one or more GPOs or TPDOs, then the following will apply:

16.14.1 Termination of License Rights. Licensee's right to sell Licensed Products to the terminated TPDOs, the terminated GPO, or the IDOs that are members of the terminated GPO will terminate, and without limitation, for the purposes of this Agreement: (a) TPDO Clinics of the terminated TPDO will cease to be Authorized Dialysis Centers; (b) IDOs that are members of the Terminated GPO will cease to be IDOs, and IDO Clinics of such IDOs will cease to be Authorized Dialysis Centers.

16.14.2 Cessation of Sales. Licensee will cease all sales of Licensed Product to the terminated TPDO and its TPDO Clinics and to the terminated GPO, its IDO members, and the IDO Clinics of such IDO members.

16.15. Suspension of Licensed Rights. Promptly following the commencement of any Suspension Period (as set forth under Section 3.2.2 (Suspension)), Licensee will [**]. During any Suspension Period the Articles and Sections set forth in Section 16.16 (Survival; Accrued Rights) will survive. Upon the commencement of any Suspension Period, if and only if sales of Licensed

Products have commenced, Akebia will [**] at a [**] of [**]% of [**]. Except as provided in this Section 16.14 (Suspension of Licensed Rights) and Section 16.16 (Survival; Accrued Rights), during the Suspension Period, all other rights and obligations of the Parties pursuant to the License will be suspended and be of no force and effect.

16.16. Survival; Accrued Rights. The following Articles and Sections of this Agreement will survive suspension of the License or expiration or early termination of the Agreement for any reason: Section 9.1 (Trademark Responsibility), Section 9.3 (Trademark Ownership and Cooperation), Section 11.4 (Sales Reports), but only with respect to Net Sales made during the Term, Section 11.7 (Accounting), Section 11.8 (Methods of Payment), Section 11.9 (Late Payments), Section 13.7 (Limitation of Liability), Article 14 (Confidentiality), Article 15 (Indemnification), other than Section 15.5 (Insurance), Section 16.10.1 (Termination Fee), Section 16.10.2 (Commercialization of Competing Product), Section 16.11 (Termination Following Bundle Exclusion) (with respect to payment obligations set forth therein), Section 16.13 (Effects of Termination), this Section 16.16 (Survival; Accrued Rights), Article 17 (Dispute Resolution; Governing Law), and Article 18 (Miscellaneous). In any event, suspension of the License or expiration or termination of this Agreement will not relieve the Parties of any liability that accrued hereunder prior to the effective date of such suspension, expiration or termination (including Licensee's obligation to pay Akebia pursuant to Article 11 (Payments) with respect to sales made prior to such suspension, expiration or termination), nor preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity with respect to any breach of this Agreement, nor prejudice either Party's right to obtain performance of any obligation.

Article 17

DISPUTE RESOLUTION; GOVERNING LAW

17.1. Executive Officers. Unless otherwise set forth in this Agreement, in the event of a dispute arising under this Agreement between the Parties, the Parties will refer such dispute to their respective chief executive officers, and such chief executive officers will attempt in good faith to resolve such dispute.

17.2. Litigation. Any unresolved dispute which was subject to Section 17.1 (Executive Officers) must be brought exclusively in a court of competent jurisdiction, federal or state, located in the State of New York, and in no other jurisdiction. Each Party hereby consents to personal jurisdiction and venue in, and agrees to service of process issued or authorized by, such court.

17.3. Jurisdiction. Each Party to this Agreement, by its execution hereof, (a) hereby irrevocably submits to the exclusive jurisdiction of the United States District Court for the Southern District of New York and state courts located in New York, New York for the purpose of any and all unresolved disputes which were subject to Section 17.1 (Executive Officers), (b) hereby waives to the extent not prohibited by Applicable Law, and agrees not to assert, by way of motion, as a defense or otherwise, in any such action, any claim that it is not subject personally to the jurisdiction of the above-named courts, that its property is exempt or immune from attachment or execution, that any such action brought in one of the above-named courts in such jurisdiction should be dismissed on grounds of *forum non conveniens*, should be transferred to any court other than one of the above-named courts, or should be stayed by reason of the pendency of some other proceeding in any other court other than one of the above-named courts, or that this Agreement or the subject matter hereof may not be enforced in or by such court, and (c) hereby agrees not to commence any such action other than before one of the above-named courts nor to make any motion or take any other action seeking or intending to cause the transfer or removal of any such action to any court other than one of the above-named courts whether on the grounds of inconvenient forum or otherwise. Notwithstanding the foregoing, application may be made to any court of competent jurisdiction with respect to the enforcement of any judgment or award.

17.4. Governing Law. This Agreement will be governed by and construed in accordance with the laws of the State of New York, without reference to conflict of law principles.

17.5. Injunctive Relief. Notwithstanding the foregoing, in the event of an actual or threatened breach hereunder, the aggrieved Party may seek equitable relief (including restraining orders, specific performance, or other injunctive relief) in any court or other forum, without first submitting to the dispute resolution procedures set forth in Section 17.1 (Executive Officers).

Article 18

MISCELLANEOUS

18.1. Assignment. Neither Party may assign this Agreement and the licenses herein granted without the other Party's prior written consent, except that (a) Vifor may assign this Agreement to VFMCRP effective upon not less than [**] prior written notice to Akebia; or (b) either Party may assign this Agreement in its entirety in writing to a Third Party successor or purchaser of all or substantially all of the assets or businesses to which this Agreement relates whether pursuant to a sale of assets, merger, or other transaction, in which case the assigning Party will provide prior written notice to the other Party and need not obtain the other Party's consent; *provided that* the permitted assignee must assume all obligations of the assigning Party under the Agreement in writing and the assigning Party will remain fully liable for the performance of its obligations hereunder by such permitted assignee. In addition, and notwithstanding the foregoing, Akebia may assign its right to receive payments under this Agreement as part of a royalty factoring or other similar transaction undertaken for *bona fide* financing purposes. Any other assignment of this Agreement by a Party requires the prior written consent of the other Party. Any assignment in violation of this Section 18.1 (Assignment) will be null, void, and of no legal effect. This Agreement will be binding on and will inure to the benefit of the permitted successors and assigns of the Parties.

18.2. Standstill. Except in connection with the acquisition of shares by Licensee pursuant to the terms of the Investment Agreement dated as of the Original Execution Date by and between the Parties, Licensee will not, without the written consent of Akebia, acquire directly or indirectly, in a public or private transaction, including by purchase in the open market, any common stock of Akebia if the Licensee's beneficial ownership of the common stock of Akebia would thereafter exceed [**]%. In addition, unless approved in advance in writing by Akebia, Licensee will not, directly or indirectly:

(a) Make any statement or proposal to Akebia, other than a non-public statement or proposal delivered directly to the chief executive officer or chairman of the board of directors, or to any of Akebia's stockholders regarding, or make any public announcement, proposal, or offer (including a "solicitation" of "proxies" as such terms are defined or used in Regulation 14A of the Exchange Act) with respect to, or otherwise solicit, seek, or offer to effect (including, for the avoidance of doubt, indirectly by means of communication with the press or media) (i) any business combination, merger, tender offer, exchange offer, or similar transaction involving Akebia, (ii) any restructuring, recapitalization, liquidation, or similar transaction involving Akebia, (iii) any acquisition of any of Akebia's equity securities or assets or rights or options to acquire equity securities or assets, (iv) any proposal to seek representation on the board of directors of Akebia or otherwise seek to control or influence the management, board of directors, or policies of Akebia, or (v) any proposal, arrangement, or other statement that is inconsistent with this Section 18.2 (Standstill);

(b) Instigate, encourage, or assist any Third Party (including forming a "group" with any such Third Party) to do, or enter into any discussions or agreements with any Third Party with respect to, any of the actions set forth in Section 18.2 (Standstill); or

(c) Take any action that would reasonably be expected to require Akebia or any of its Affiliates to make a public announcement regarding any of the actions set forth in Section 18.2 (Standstill).

Notwithstanding the foregoing provisions, the restrictions set forth in this Section 18.2 (Standstill) will terminate and be of no further force and effect (a) [**], *provided that* the provisions of this Section 18.2 (Standstill) will be revived if such [**]; or (b) upon the expiration or termination of this Agreement. For the avoidance of doubt, nothing in this Section 18.2 (Standstill) will prohibit Licensee from acquiring beneficial ownership of the common stock of Akebia to the extent such ownership remains less than [**]% of Akebia's total outstanding common stock. For purposes of this Section 18.2 (Standstill), "**Sale Transaction**" means a transaction between Akebia and a Third Party (i) involving the direct or indirect acquisition by such Third Party of [**]% or more of Akebia's outstanding shares of common stock or consolidated assets (including assets held by subsidiaries), *excluding* a transaction in which (A) [**], or (B) [**], or (ii) involving the sale of substantially all of Akebia's rights with respect to the Licensed Products.

18.3. **Force Majeure**. If either Party will be delayed, interrupted in, or prevented from the performance of any obligation hereunder by reason of any cause beyond its reasonable control, including an act of God, fire, flood, earthquake, war (declared or undeclared), public disaster, epidemic, act of terrorism, or strikes (other than strikes of a Party's own employees), then such Party will not be liable to the other therefor; and the time for performance of such obligation will be extended for a period equal to the duration of the force majeure that occasioned the delay, interruption, or prevention. The Party invoking such force majeure rights of this Section 18.3 (Force Majeure) must notify the other Party by courier or overnight dispatch (*e.g.*, Federal Express) no later than 30 days after each of the first and last day of the force majeure unless the force majeure renders such notification impossible, in which case notification will be made as soon as possible. If the delay resulting from the force majeure exceeds three months, then the Party not affected by the force majeure will have the right to terminate this Agreement forthwith pursuant to Section 16.2 (Termination for Breach) with the consequences set out in Section 16.13 (Effects of Termination), as if the Party affected by the force majeure were in material breach of this Agreement.

18.4. **Entire Agreement**. This Agreement, together with exhibits and schedules attached hereto, (a) constitutes the entire agreement between the Parties with respect to the subject matter hereof, (b) amends and restates the First Amended Agreement in its entirety, and (c) supersedes all prior understandings of the Parties with respect thereto (including the Original Agreement, the First Amended Agreement and that certain Confidential Disclosure Agreement between the Parties dated [**], as amended by Amendment No. 1 dated [**]) and will not be modified, amended, or terminated, except as herein provided or except by another agreement in writing executed by the Parties.

18.5. **Severability**. If any provision of this Agreement is declared invalid by a court of last resort or by any court or other governmental body from the decision of which an appeal is not taken within the time provided by law, then and in such event, this Agreement will be deemed to have been terminated only as to the portion thereof that relates to the provision invalidated by that decision and only in the relevant jurisdiction, but this Agreement, in all other respects and all other jurisdictions, will remain in force; *provided*, *however*, that if the provision so invalidated is essential to the Agreement as a whole, then the Parties will negotiate in good faith to amend the terms hereof as nearly as practical to carry out the original intent of the Parties, and, failing to agree to such amendment, then either Party may submit the matter for resolution pursuant to Article 17 (Dispute Resolution; Governing Law).

18.6. **Notices**. Any notice or report required or permitted to be given under this Agreement will be in writing and will be mailed by internationally recognized express delivery service, or sent by email or facsimile and confirmed by mailing, as follows:

If to Akebia:

Akebia Therapeutics, Inc.
245 First Street
Cambridge, MA 02142

Attention: Chief Executive Officer
Facsimile: [**]
Email: [**]

With copies to (which will not constitute notice for purposes of this Agreement):

Akebia Therapeutics, Inc.
245 First Street
Cambridge, MA 02142
Attention: Senior Vice President, Chief Legal Officer and Secretary
Facsimile: [**]
Email: [**]

and

Ropes & Gray LLP
Prudential Tower, 800 Boylston Street
Boston, MA 02199-3600
Attention: [**]
Facsimile: [**]
Email: [**]

If to Licensee:

Vifor Pharma Management Ltd.
Flughofstrasse 61, 8152 Glattbrugg, Switzerland
Attention: [**]
Facsimile: [**]
Email: [**]

With a copy to (which will not constitute notice for purposes of this Agreement):

Vifor Pharma Management Ltd
Flughofstrasse 61, 8152 Glattbrugg, Switzerland
Facsimile: [**]
Attention: [**]
Email: [**]

18.7. **Further Assurances**. The Parties agree to reasonably cooperate with each other in connection with any actions required to be taken as part of their respective obligations under this Agreement, and will (a) furnish to each other such further information; (b) execute and deliver to each other such other documents; and (c) do such other acts and things (including working collaboratively to correct any clerical, typographical, or other similar errors in this Agreement), all as the other Party may reasonably request for the purpose of carrying out the intent of this Agreement.

18.8. **Agency**. Neither Party is, nor will be deemed to be an employee, agent, or representative of the other Party for any purpose. Each Party is an independent contractor, not an employee or partner of the other Party. Neither Party will have the authority to speak for, represent, or obligate the other Party in any way without prior written authorization from the other Party.

18.9. **No Waiver**. Any omission or delay by either Party at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants, or provisions hereof, by the other Party, will not constitute a waiver of such Party's rights to the future enforcement of its rights under this Agreement. Any waiver by a Party of a particular breach or default by the other Party will not operate or be construed as a waiver of any subsequent breach or default by the other Party.

18.10. Interpretation. (a) Whenever any provision of this Agreement uses the term "including" (or "includes"), such term will be deemed to mean "including without limitation" and "including but not limited to" (or "includes without limitations" and "includes but is not limited to") regardless of whether the words "without limitation" or "but not limited to" actually follow the term "including" (or "includes"); (b) "herein," "hereby," "hereunder," "hereof," and other equivalent words will refer to this Agreement in its entirety and not solely to the particular portion of this Agreement in which any such word is used; (c) all definitions set forth herein will be deemed applicable whether the words defined are used herein in the singular or the plural; (d) wherever used herein, any pronoun or pronouns will be deemed to include both the singular and plural and to cover all genders; (e) the recitals set forth at the start of this Agreement, along with the schedules and exhibits to this Agreement, and the terms and conditions incorporated in such recitals and schedules and exhibits will be deemed integral parts of this Agreement and all references in this Agreement to this Agreement will encompass such recitals and schedules and exhibits and the terms and conditions incorporated in such recitals and schedules and exhibits; *provided that* in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions set forth in the recitals, schedules, or exhibits, the terms of this Agreement will control; (f) in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions that may be set forth on any order, invoice, verbal agreement, or otherwise, the terms and conditions of this Agreement will govern; (g) this Agreement will be construed as if both Parties drafted it jointly, and will not be construed against either Party as principal drafter; (h) unless otherwise provided, all references to Sections, Articles, and Schedules in this Agreement are to Sections, Articles, and Schedules of and to this Agreement; (i) any reference to any federal, national, state, local, or foreign statute or law will be deemed to also refer to all rules and regulations promulgated thereunder, unless the context requires otherwise; (j) wherever used, the word "shall" and the word "will" are each understood to be imperative or mandatory in nature and are interchangeable with one another; (k) the word "or" will not be exclusive; (l) references to a particular person include such person's successors and assigns to the extent not prohibited by this Agreement; and (m) the section headings and captions used herein are inserted for convenience of reference only and will not be construed to create obligations, benefits, or limitations.

18.11. Cumulative Remedies. No remedy referred to in this Agreement is intended to be exclusive, but each will be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law.

18.12. Counterparts. This Agreement may be executed in counterparts, all of which taken together will be regarded as one and the same instrument. This Agreement may be executed by facsimile, .pdf, or other electronically transmitted signatures and such signatures will be deemed to bind each Party hereto as if they were the original signatures.

[Remainder of page intentionally left blank; signature page follows.]

IN WITNESS WHEREOF, the Parties have executed this Second Amended Agreement through their duly authorized representatives to be effective as of the Effective Date.

AKEBIA THERAPEUTICS, INC. VIFOR (INTERNATIONAL) LTD.

By: /s/ John P. Butler By: /s/ Dr. Christoph Springer

Name: John P. Butler Name: Dr. Christoph Springer

Title: President and Chief Executive Officer Title: Chief Strategy Officer

VIFOR (INTERNATIONAL) LTD.

By: /s/ Dr. Oliver P. Kronenberg

Name: Dr. Oliver P. Kronenberg

Title: Group General Counsel

Exhibit 10.58

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Triple asterisks denote omission.

Master Manufacturing Services Agreement

September 27, 2016

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MASTER MANUFACTURING SERVICES AGREEMENT

THIS MASTER MANUFACTURING SERVICES AGREEMENT (the "Agreement") is made as of September 27, 2016 (the "**Effective Date**")

B E T W E E N:

PATHEON MANUFACTURING SERVICES LLC,
a limited liability company existing under the laws of the State of Delaware

("**Patheon**"),

- and -

KERYX BIOPHARMACEUTICALS, INC.
a corporation existing under the laws of the State of Delaware

("**Client**").

THIS AGREEMENT WITNESSES THAT in consideration of the rights conferred and the obligations assumed herein, and for other good and valuable consideration (the receipt and sufficiency of which are acknowledged by each party), and intending to be legally bound the parties agree as follows:

ARTICLE 1
STRUCTURE OF AGREEMENT AND INTERPRETATION

1.1 Master Agreement.

This Agreement establishes the general terms and conditions under which Patheon or any Affiliate of Patheon may perform Manufacturing Services for Client or any Affiliate of Client, at the manufacturing site where Patheon or the Affiliate of Patheon resides. This "master" form of agreement is intended to allow the parties, or any of their Affiliates, to contract for the manufacture of multiple Products through Patheon's global network of manufacturing sites through the issuance of site specific Product Agreements without having to re-negotiate the basic terms and conditions contained herein.

1.2 Product Agreements.

This Agreement is structured so that a Product Agreement may be entered into by the parties for the manufacture of a particular Product or multiple Products at a Patheon manufacturing site. Each Product Agreement will be governed by the terms and conditions of this Agreement unless the parties to the Product Agreement expressly modify the terms and conditions of this Agreement in the Product Agreement. Unless otherwise agreed by the parties, each Product Agreement will be in the general form and contain the information set forth in Appendix 1 hereto.

1.3 Definitions.

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The following terms will, unless the context otherwise requires, have the respective meanings set out below and grammatical variations of these terms will have corresponding meanings:

"**Active Materials**", **"Active Pharmaceutical Ingredients" or "API"** means the materials listed in a Product Agreement on Schedule D;

"**Active Materials Credit Value**" means the value of the Active Materials for certain purposes of this Agreement, as set forth in a Product Agreement on Schedule D;

"**Actual Annual Yield**" or "**AAY**" has the meaning specified in Section 2.2(a);

"**Affiliate**" means:

(a) a business entity which owns, directly or indirectly, a controlling interest in a party to this Agreement, by stock ownership or otherwise; or

(b) a business entity which is controlled by a party to this Agreement, either directly or indirectly, by stock ownership or otherwise; or

(c) a business entity, the controlling interest of which is directly or indirectly common to the majority ownership of a party to this Agreement;

For this definition, "control" means the ownership of shares carrying at least a majority of the votes for the election of the directors of a corporation;

"Annual Product Review Report" means the annual product review report prepared by Patheon as described in Title 21 of the United States Code of Federal Regulations, Section 211.180(e);

"**Annual Report"** means the annual report to the FDA prepared by Client regarding the Product as described in Title 21 of the United States Code of Federal Regulations, Section 314.81(b)(2);

"**Annual Volume**" means the minimum volume of Product to be manufactured in any Year of this Agreement as set forth in Schedule B;

"**Applicable Laws**" means (i) for Patheon, all Laws, including, without limitation, (A) those of the State of North Carolina or the local jurisdiction for Patheon Affiliate, in any event being the jurisdiction where the Manufacturing Site is located, and (B) FDA and EMA regulations, governing or related to any and all activities of Patheon and its Affiliates under this Agreement; and (ii) for Client and the Products, the Laws of all jurisdictions where the Products are manufactured, distributed, and marketed as these are agreed and understood by the parties in this Agreement;

"**Authority**" means any governmental or regulatory authority, subdivision, department, body or agency or any court, tribunal, bureau, commission or other similar body, whether federal, state, provincial, county or municipal;

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“**Breach Notice**” has the meaning specified in Section 8.2(a);

"**Business Day**" means a day other than a Saturday, Sunday or a day that is a statutory holiday in the jurisdiction of the applicable manufacturing site;

“**Capital Equipment Agreement**” means a separate agreement that the parties may enter into that will address responsibility for the purchase of capital equipment and facility modifications that may be required to perform the Manufacturing Services under a particular Product Agreement;

"**cGMPs**" means, as applicable, current good manufacturing practices as described in:

(a) Parts 210 and 211 of Title 21 of the United States' Code of Federal Regulations;

(b) EC Directive 2003/94/EC; and

(c) Division 2 of Part C of the *Food and Drug Regulations* (Canada);

together with the latest Health Canada, FDA and EMA guidance documents pertaining to manufacturing and quality control practice, all as updated, amended and revised from time to time;

“Client Intellectual Property” means (a) Intellectual Property of Client existing prior to the Effective Date, including but not limited to, inventions, ideas, discoveries, developments, technical information, know-how and confidential information existing prior to the Effective Date, (b) Intellectual Property that is developed, discovered or created outside of either Party’s performance under this Agreement which is specific to, or dependent upon, Client’s Active Material, Product, and/or any Client Confidential Information, and (c) Intellectual Property that is developed, discovered, or created in connection with this Agreement which is specific to, or dependent upon, Client’s Active Material, Product, and/or any Client Confidential Information.

“**Client Property**” has the meaning specified in Section 8.4(e);

“**Client-Supplied Components**” means those Components to be supplied by Client or that have been supplied by Client, excluding the API;

“**CMC**” has the meaning specified in Section 7.8(c);

"**Components**" means, collectively, all packaging components, raw materials, ingredients, and other materials (including labels, product inserts and other labelling for the Products) required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

“**Confidential Information**” has the meaning specified in Section 11.1;

“**Deficiencies**” have the meaning specified in Section 7.8(d);

"**Deficiency Notice**" has the meaning specified in Section 6.1(a);

“Delivery Date” means the date scheduled for shipment of Product under a Firm Order as set forth in Section 5.1(d);

“Disclosing Party” has the meaning specified in Section 11.1;

"**EMA**" means the European Medicines Agency;

"**FDA**" means the United States Food and Drug Administration;

"**Firm Orders**" have the meaning specified in Section 5.1(c);

“**Force Majeure Event**” has the meaning specified in Section 13.7;

"**GST**" has the meaning specified in Section 13.16(a)(ii);

"**Health Canada**" means the section of the Canadian Government known as Health Canada and includes, among other departments, the Therapeutic Products Directorate and the Health Products and Food Branch Inspectorate;

“**Importer of Record**” has the meaning specified in Section 3.2(a);

“**Initial Product Term**” has the meaning specified in Section 8.1;

“**Initial Set Exchange Rate**” means as of the Effective Date of a Product Agreement, the initial exchange rate set forth in the Product Agreement to convert one unit of the billing currency into the Patheon Manufacturing Site local currency, calculated as the daily average interbank exchange rate for conversion of one unit of the billing currency into the Patheon Manufacturing Site local currency during the 90 day period immediately preceding the Effective Date as published by OANDA.com “The Currency Site” under the heading “FxHistory: historical currency exchange rates” at www.OANDA.com/convert/fxhistory;

“**Initial Term**” has the meaning specified in Section 8.1;

"**Intellectual Property**" includes, without limitation, rights in patents, patent applications, formulae, trademarks, process, trademark applications, trade-names, Inventions, copyrights, industrial designs, trade secrets, and know how;

"**Invention**" means information about any innovation, improvement, development, discovery, computer program, device, trade secret, method, know-how, process, technique or the like, whether or not written or otherwise fixed in any form or medium, regardless of the media on which it is contained and whether or not patentable or copyrightable;

"**Inventory**" means all inventories of Components and work-in-process produced or held by Patheon for the manufacture of the Products but, for greater certainty, does not include the Active Materials;

"**Laws**" means all laws, statutes, ordinances, regulations, rules, by-laws, judgments, decrees or orders of any Authority;

“Long Term Forecast” has the meaning specified in Section 5.1(a);

"**Manufacturing Services**" means the manufacturing, quality control, quality assurance, analytical testing, stability testing, packaging, and related services, as set forth in this Agreement, required to manufacture Product or Products using the Active Materials and Components;

"**Manufacturing Site**" means the facility owned and operated by Patheon where the Manufacturing Services will be performed as identified in a Product Agreement;

“Materials” means all Components and other items required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

"**Maximum Credit Value**" means the maximum value of Active Materials that may be credited by Patheon under this Agreement, as set forth in a Product Agreement on Schedule D;

“**Minimum Market Requirement**” means the minimum percentage of Client’s or its Affiliates’ requirements for a Product in the Territory, if any, that must be purchased from Patheon or its Affiliates.

"**Minimum Order Quantity**" means the minimum number of batches of a Product to be produced during the same cycle of manufacturing as set forth in a Product Agreement on Schedule B;

“**Obsolete Stock**” has the meaning specified in Section 5.2(b);

“**Competitor**” means (a) in the case of Patheon, a business that derives greater than 50% of its revenues from performing contract pharmaceutical development or commercial manufacturing services and (b) in the case of Client, a business whose primary focus is the research, development and/or commercialization of products that are competitive with the Products;

“Patheon Intellectual Property” means Intellectual Property generated or derived by Patheon before performing any Manufacturing Services, developed by Patheon while performing the Manufacturing Services, or otherwise generated or derived by Patheon in its business which Intellectual Property is not specific to or dependent upon, Client’s Active Material, Product, and/or Client Confidential Information, including, without limitation, Inventions and Intellectual Property which may apply to manufacturing processes or the formulation or development of drug products, drug product dosage forms or drug delivery systems unrelated to the specific requirements of the Product(s);

“**Persistent Supply Failure**” means Patheon’s failure to supply at least [***] of the quantity of Product ordered by Client (i) for [***] or longer of any forecast period; or (iii) on [***] or more orders during a Year.

“**PPI**” has the meaning specified in Section 4.2(a);

“Price” means the price measured in US Dollars to be charged by Patheon for performing the Manufacturing Services, and includes the cost of Components (other than Client-Supplied Components), certain cost items as set forth in a Product Agreement on Schedule B, and annual stability testing costs as set forth in a Product Agreement on Schedule C;

"**Product(s)**" means the product(s) listed in a Product Agreement on Schedule A;

"**Product Agreement**" means the agreement between Patheon and Client issued under this Agreement in the form set forth in Appendix 1 (including Schedules A to E) under which Patheon will perform Manufacturing Services at a particular Manufacturing Site;
"**Product Claims**" have the meaning specified in Section 6.3(d);

"**Quality Agreement**" means the agreement (the general form of which is set forth in Exhibit B) between the parties entering a Product Agreement that sets out the quality assurance standards for the Manufacturing Services to be performed by Patheon for Client;

"**Recall**" has the meaning specified in Section 6.2(a);

"**Recipient**" has the meaning specified in Section 11.1;

"**Regulatory Authority**" means the FDA, EMA, and Health Canada and any other foreign regulatory agencies or Authorities competent to grant marketing approvals for pharmaceutical products including the Products in the Territory;

"**Remediation Period**" has the meaning specified in Section 8.2(a);

"**Representatives**" means a party's directors, officers, employees, advisers, agents, consultants, subcontractors, service partners, professional advisors, or representatives;
"Resident Jurisdiction" has the meaning specified in Section 13.16(a)(i);

"Set Exchange Rate" means the exchange rate to convert one unit of the billing currency into the Patheon Manufacturing Site local currency for each Year, calculated as the average daily interbank exchange rate for conversion of one unit of the billing currency into the Patheon Manufacturing Site local currency during the full year period (October 1st [preceding year] to September 30th) as published by OANDA.com "The Currency Site" under the heading "FxHistory: historical currency exchange rates" at www.OANDA.com/convert/fxhistory;

"**Shortfall Credit**" has the meaning specified in Section 2.2(b);

"**Specifications**" means the file, for each Product, which is given by Client to Patheon in accordance with the procedures listed in a Product Agreement on Schedule A and which contains documents relating to each Product, including, without limitation:

(a) specifications for Active Materials and Components;

(b) manufacturing specifications, directions, and processes;

(c) storage requirements;

(d) all environmental, health and safety information for each Product including material safety data sheets; and

(e) the finished Product specifications, packaging specifications and shipping requirements for each Product;

all as updated, amended and revised from time to time by Client in accordance with the terms of this Agreement;

"**Surplus**" has the meaning specified in Section 2.2(c);

"**Target Yield**" has the meaning specified in Section 2.2(a);

"**Tax**" or "**Taxes**" have the meaning specified in Section 13.16(a);

"**Technical Dispute**" has the meaning specified in Section 12.2;

"**Territory**" means the geographic area described in a Product Agreement where Products manufactured by Patheon will be distributed by Client;

"**Third Party Rights**" means the Intellectual Property of any third party;

"**VAT**" has the meaning specified in Section 13.16(d);

"**Year**" means in the first year of this Agreement or in the first year of a Product Agreement, the period from the Effective Date up to and including December 31 of the same calendar year, and thereafter will mean a calendar year.

"Yield Tolerance" has the meaning specified in Section 2.2(b); and

"**Zero Forecast Period**" has the meaning specified in Section 5.1(g).

1.4 Currency.

Unless otherwise agreed in a Product Agreement, all monetary amounts expressed in this Agreement are in United States Dollars (USD).

1.5 Sections and Headings.

The division of this Agreement into Articles, Sections, Subsections, and Appendix, Schedules and Exhibits and the insertion of headings are for convenience of reference only and will not affect the interpretation of this Agreement. Unless otherwise indicated, any reference in this Agreement to a Section, Appendix, Schedule or Exhibit refers to the specified Section, Appendix, Schedule or Exhibit to this Agreement. In this Agreement, the terms "**this Agreement**", "**hereof**", "**herein**", "**hereunder**" and similar expressions refer to this Agreement as a whole and not to any particular part, Section, Appendix, Schedule or Exhibit of this Agreement.

1.6 Singular Terms.

Except as otherwise expressly stated or unless the context otherwise requires, all references to the singular will include the plural and vice versa.

1.7 Appendix 1, Schedules and Exhibits.

Appendix 1 (including the Schedules thereto) and the following Exhibits are attached to, incorporated in, and form part of this Agreement:

Appendix 1 - Form of Product Agreement (Including Schedules A to E)

Exhibit A	- Technical Dispute Resolution
Exhibit B	- Commercial Quality Agreement
Exhibit C	- Monthly Active Materials Inventory Report
Exhibit D	- Report of Annual Active Materials Inventory Reconciliation and Calculation of Actual Annual Yield
Exhibit E	- Example of Price Adjustment Due to Currency Fluctuation

ARTICLE 2
PATHEON'S MANUFACTURING SERVICES

2.1 Manufacturing Services.

Patheon will perform the Manufacturing Services for the Territory for the fees specified in a Product Agreement in Schedules B and C to manufacture Products for Client. Schedule B to a Product Agreement sets forth a list of cost items that are included or not included in the Price for Products; all cost items that are not included in the Price are subject to additional fees to be paid by the Client. Patheon may amend the fees set out in Schedules B and C to a Product Agreement as set forth in Article 4. Patheon may change the Manufacturing Site for the Products only with the prior written consent of Client, this consent not to be unreasonably withheld. Unless otherwise agreed in a Product Agreement, the Minimum Market Requirement shall be [***] of Client's annual commercial requirements for Products offered for sale in the Territory for any Year. Patheon shall have the right, and the obligation, to supply the Minimum Market Requirement, provided that the Minimum Market Requirement shall be reduced to [***] in the event of any Persistent Supply Failure. Subject to any applicable Minimum Market Requirement, this Agreement is non-exclusive and nothing in this Agreement shall prevent Client from obtaining services from third parties that are equivalent or similar to the Manufacturing Services. To the extent specified in a Product Agreement, Patheon will be entitled to any applicable manufacturing tax credits that arise from performing the Manufacturing Services under this Agreement. In performing the Manufacturing Services, Patheon and Client agree that:

(a) Conversion of Active Materials and Components. Patheon will convert Active Materials and Components into Products.

(b) Quality Control and Quality Assurance. Patheon will perform the quality control and quality assurance testing specified in the Quality Agreement. Batch review and release to Client will be the responsibility of Patheon's quality assurance group. Patheon will perform its batch review and release responsibilities in accordance with Patheon's standard operating procedures. Prior to shipment of Products to Client, Patheon will provide to Client a certificate of analysis, certificate of origin (BSE / TSE statement) and a certificate of compliance, including a statement that the batch has been manufactured and tested in accordance with Specifications and cGMPs. Client Quality Assurance will review such documents prior to release. For routine or standard batches with no major issues or only minor deviations, Client will use good faith efforts to release the batches within 5 Business Days, or as otherwise agreed. Client will have sole responsibility to authorize a shipment from the manufacturing site and for the release of Products to the market. The form and style of batch documents, including, but not limited to, batch production records, lot packaging records, equipment set up control, operating parameters, and data printouts, raw material data, and laboratory notebooks are the exclusive property of Patheon. Specific Product related information contained in those batch documents is Client property. Notwithstanding the foregoing, Client may make reasonable requests and shall be entitled to review the raw testing data, and other information set forth in the Quality Agreement.

(c) Components. Patheon will purchase and test all Components (with the exception of Client-Supplied Components) at Patheon's expense and as required by the Specifications.

(d) Stability Testing. Patheon will conduct stability testing on the Products in accordance with the protocols set out in the Specifications for the separate fees and during the time periods set out in Schedule C to a Product Agreement. Patheon will not make any changes to these testing protocols without prior written approval from Client. If a confirmed stability test failure occurs, Patheon will notify Client within one Business Day, after which Patheon and Client will jointly determine the proceedings and methods to be undertaken to investigate the cause of the failure, including which party will bear the cost of the investigation. The parties will use good faith efforts to determine the root cause of any failures and to allocate the costs. Patheon will give Client all stability test data and results at Client's request.

(e) Packaging and Artwork. Patheon will package the Products as set out in the Specifications. Client will be responsible for the cost of artwork development. Patheon will determine and imprint the batch numbers and expiration dates for each Product shipped. The batch numbers, expiration dates, serialization numbers, and 2D bar codes will be affixed on the Products and on the shipping carton of each Product as outlined in the Specifications and as required by cGMPs. Client may, in its sole discretion, make changes to labels, product inserts, and other packaging for the Products. Those changes will be submitted by Client to all applicable Regulatory Authorities and other third parties responsible for the approval of the Products. Client will be responsible for the cost of labelling obsolescence when changes occur, as contemplated in Section 4.4. Patheon's name will not appear on the label or anywhere else on the Products unless: (i) required by any Laws; or (ii) Patheon consents in writing to the use of its name. At least 90 days prior to the Delivery Date of Product for which new or modified artwork is required, Client will provide at no cost to Patheon, final camera ready artwork for all packaging Components to be used in the manufacture of the Product that meet the Specifications. For the avoidance of doubt, the parties acknowledge and agree that Client will be responsible for complying with any and all regulatory requirements for the labeling of the Product.

(f) Active Materials and Client-Supplied Components. At least [***] before the scheduled production date, Client will deliver the Active Materials and any Client-Supplied Components to the Manufacturing Site DDP (Incoterms 2010), at no cost to Patheon, in sufficient quantity to enable Patheon to manufacture the desired quantities of Product and to ship Product on the Delivery Date. If the Active Materials and/or Client-Supplied Components are not received [***] before the scheduled production date, Patheon may delay the shipment of Product by the same number of days as the delay in receipt of the Active Materials and/or Client-Supplied Components. But if Patheon is unable to manufacture Product to meet this new shipment date due to prior third party production commitments, Patheon may delay the shipment until a later date as agreed to by the parties. All shipments of Active Material will be accompanied by certificate(s) of analysis from the Active Material manufacturer and the Client, confirming the identity and purity of the Active Materials and its compliance with the Active Material specifications. For Active Materials or Client-Supplied Components which may be subject to import or export, Client agrees that its vendors and carriers will comply with applicable requirements of the U.S. Customs and Border Protection Service and the Customs Trade Partnership Against Terrorism.

(g) Intentionally omitted.

(h) Validation Activities (if applicable). Patheon shall assist in the development and approval of the validation protocols for analytical methods and manufacturing procedures (including packaging procedures) for the Products. The fees for this service are not included in the Price and will be set out separately in Schedule C to a Product Agreement.

(i) Additional Services. If Client requests services other than those expressly set forth herein or in any Product Agreement (such as qualification of a new packaging configuration or shipping studies, or validation of alternative batch sizes), Patheon will provide a good faith and reasonable written quote of the fee for the additional services and Client will advise Patheon whether it wishes to have the additional services performed by Patheon. The scope of work and fees will be set forth in a separate agreement signed by the parties. If so agreed by the parties, the terms and conditions of this Agreement will apply to these services. Such additional services or items not included in the costs may include, but are not limited to, third party supplier fees for the purchase or use of columns, standards, tooling, non-standard pallets, PAPR or PPE suits (where applicable) and other project-specific items necessary for Patheon to perform the Manufacturing Services, and which are not included as Components.

2.2 Active Material Yield.

(a) Reporting. Patheon will give Client a monthly inventory report of the Active Materials held by Patheon using the inventory report form set out in Exhibit C, which will contain the following information for the month by lot number:

Quantity Received: The total quantity of Active Materials that complies with the Specifications and is received at the Manufacturing Site during the applicable period.

Quantity Dispensed: The total quantity of Active Materials dispensed at the Manufacturing Site during the applicable period. The Quantity Dispensed is calculated by adding the Quantity Received to the inventory of Active Materials that complies with the Specifications held at the beginning of the applicable period, less the inventory of Active Materials that complies with the Specifications held at the end of the period. The Quantity Dispensed will only include Active Materials received and dispensed in commercial manufacturing of Products including Active Materials lost in the warehouse prior to and during dispensing, and will not include any [***].

Quantity Converted: The total amount of Active Materials contained in the Products manufactured with the Quantity Dispensed (including any additional Products produced in accordance with Section 6.3(a) or 6.3(b)), delivered by Patheon, and not rejected, recalled or returned in accordance with Section 6.1 or 6.2

because of Patheon's failure to perform the Manufacturing Services in accordance with Specifications, cGMPs, and Applicable Laws.

Within [***] after the end of each Year, Patheon will prepare an annual reconciliation of Active Materials on the reconciliation report form set forth in Exhibit D including the calculation of the "**Actual Annual Yield**" or "**AAY**" for the Product at the Manufacturing Site during the Year. AAY is the percentage of the Quantity Dispensed that was converted to Products and is calculated as follows:

$$\frac{\text{Quantity Converted during the Year}}{\text{Quantity Dispensed during the Year}} \times 100\%$$

After Patheon has produced a minimum of [***] successful commercial production batches of Product and has produced commercial production batches for at least [***] at the Manufacturing Site, the parties will agree on the target yield for the Product at the Manufacturing Site (each, a "**Target Yield**"). If the parties are unable to agree upon the Target Yield, they will resolve the matter pursuant to the technical dispute process set forth in Section 12.2. The Target Yield will be revised annually to reflect the actual manufacturing experience as agreed to by the parties.

(b) Shortfall Credit Calculation. If the Actual Annual Yield falls more than the Yield Tolerance (set forth in the Product Agreement) below the respective Target Yield, then the shortfall for the Year (the "**Shortfall**") will be calculated as follows:

Shortfall Credit = [(Target Yield – Yield Tolerance) – AAY] * Active Materials Credit Value * Quantity Dispensed

(c) Surplus Calculation. If the Actual Annual Yield is more than the respective Target Yield in a Year, then the surplus for that Year (the "Surplus") will be determined based on the following calculation:

Surplus = [AAY -- Target Yield] * Active Materials Credit Value * Quantity Dispensed

(d) Credits.

Credit for Shortfall. If there is a Shortfall for a Product in a Year, then Patheon will credit Client's account for the amount of the Shortfall not later than [***] after the end of the Year. Each credit under this Section 2.2(d) will be summarized on the reconciliation report form set forth in Exhibit D. Upon expiration or termination of a Product Agreement, any remaining credit owing under this Section will be paid to Client. The Annual Shortfall, if any, will be disclosed by Patheon on the reconciliation report form.

Surplus Credit. If there is a Surplus for a Product in a Year, then Patheon will be entitled to apply the amount of the Surplus as a credit against any Shortfall for that Product which may occur in the next Year. If there is no Shortfall in the next Year the Surplus credit will expire.

Each credit under this Section 2.2 will be summarized on the reconciliation report prepared in the form set forth in Exhibit D. Upon expiration or termination of a Product Agreement, any remaining Shortfall credit amount owing under this Section 2.2 will be paid to Client.

(e) Maximum Credit. Patheon's liability for Active Materials calculated in accordance with this Section 2.2 for any Product in a Year will not exceed, in the aggregate, the Maximum Credit Value set forth in Schedule D to a Product Agreement.

(f) No Material Breach. It will not be a material breach of this Agreement by Patheon under Section 8.2(a) solely because the Actual Annual Yield is less than the Target Yield, so long as the Shortfall is not the result of Patheon failing to meet any obligation set forth in this Agreement.

ARTICLE 3
CLIENT'S OBLIGATIONS

3.1 Payment.

Client will pay Patheon for performing the Manufacturing Services according to the Prices specified in Schedules B and C in a Product Agreement. These Prices may be subject to adjustment under other parts of this Agreement.

3.2 Active Materials and Qualification of Additional Sources of Supply.

(a) Client will at its sole cost and expense deliver the Active Materials to Patheon in accordance with Section 2.1(f). If applicable, Patheon and the Client will reasonably cooperate to permit the import of the Active Materials to the Manufacturing Site. Client's obligation will include obtaining the proper release of the Active Materials from the applicable Customs Agency and Regulatory Authority. Client or Client's designated broker will be the "**Importer of Record**" for Active Materials imported to the Manufacturing Site. The Active Materials will be held by Patheon on behalf of Client as set forth in this Agreement. Title to the Active Materials will at all times remain the property of Client. Any Active Materials received by Patheon will only be used by Patheon to perform the Manufacturing Services. Client will be responsible for paying for all rejected Product that arises from defects in the Active Materials which could not be reasonably discoverable by Patheon using the test methods set forth in the Specifications.

(b) If Client asks Patheon to qualify an additional source for the Active Material or any Component, Patheon may agree to evaluate the Active Material or Component to be supplied by the additional source to determine if it is suitable for use in the Product. The parties will agree on the scope of work to be performed by Patheon at Client's cost. For an Active Material, this work may include: (i) laboratory testing to confirm the Active Material meets existing specifications; (ii) manufacture of an experimental batch of Product that will be placed on three months accelerated stability; and (iii) manufacture of three full-scale validation batches that will be placed on concurrent stability (one batch may be the registration batch if manufactured at full scale). Section 6.1(d) will apply to all Product manufactured using the newly approved Active Material or Component because of the limited material characterization that is performed on additional sources of supply.

(b) Patheon will promptly advise Client if it encounters supply problems, including delays and/or delivery of non-conforming Active Material or Components from a Client designated additional source; and (ii) Patheon and Client will cooperate to reduce or eliminate any supply problems from these additional sources of supply. Client will be obligated to certify all Client designated sources of supply on an annual basis at its expense and will provide Patheon with copies of these annual certifications, as further set forth in the Quality Agreement, and pursuant to Patheon's standard certification form. If Patheon agrees to certify a Client designated additional sources of supply on behalf of Client, it will do so at Client's expense.

ARTICLE 4
CONVERSION FEES AND COMPONENT COSTS

4.1 First Year Pricing.

The Price for the first Year will be listed in Schedules B and C in a Product Agreement and will be subject to the adjustments set forth in Sections 4.2 and 4.3. The Price may also be increased or decreased by Patheon at any time upon written notice to Client if there are changes to the underlying manufacturing, packaging or testing assumptions set forth in Schedule B of the Product Agreement that result in an increase or decrease in the cost of performing the Manufacturing Services. Patheon shall provide documentation as to why such Price for the first year is being increased or decreased; provided however, Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers.

4.2 Price Adjustments – Subsequent Years' Pricing.

After the first Year of the Product Agreement, Patheon may adjust the Price effective January 1st of each Year as follows:

(a) Manufacturing and Stability Testing Costs. For Products manufactured in the United States or Puerto Rico, Patheon may adjust the conversion component of the Price and the annual stability testing costs for inflation, based upon the preliminary number for any increase in the Producer Price Index pcu325412325412 for Pharmaceutical Preparation Manufacturing ("**PPI**") published by the United States Department of Labor, Bureau of Labor Statistics in August of the preceding Year compared to the final number for the same month of the Year prior to that, unless the parties otherwise agree in writing. On or before [***], Patheon will give Client a statement setting forth the calculation for the inflation adjustment to be applied in calculating the Price for the next Year. For Products manufactured outside the United States or Puerto Rico, Patheon may similarly adjust the Price for inflation using an inflation index to be agreed by the parties in a Product Agreement.

(b) Component Costs. If Patheon incurs an increase in Component costs during the Year, it may increase the Price for the next Year to pass through the additional Component costs at Patheon's actual cost. If Patheon obtains a decrease in Component costs during the Year, it will decrease the Price for the next Year to pass through [***] of the cost savings to the Client. On or before [***], Patheon will give Client information about the increase or decrease in Component costs which will be applied to the calculation of the Price for the next Year to reasonably demonstrate that the Price increase or decrease is justified. But Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers.

(c) Pricing Basis. Client acknowledges that the Price in any Year is quoted based upon the Minimum Order Quantity and the Annual Volume specified in Schedule B to a Product Agreement. The Price is subject to change if the specified Minimum Order Quantity changes or if the Annual Volume is not ordered in a Year. For greater certainty, if Patheon and Client agree that the Minimum Order Quantity will be reduced or the Annual Volume in the lowest tier will not be ordered in a Year whether as a result of a decrease in estimated Annual Volume or otherwise and, as a result of the reduction, Patheon demonstrates to Client that its costs to perform the Manufacturing Services or to acquire the Components for the Product will increase on a per unit basis (including the amount of the increase), then Patheon may increase the Price by an amount sufficient to absorb the documented increased costs. On or before [***], Patheon will give Client a statement and sufficient justification setting forth the information to be applied in calculating those cost increases for the next Year, and the parties will use good faith efforts to approve any such increases. Such cost increase must be approved by Client in advance of cost increases going into effect; provided however, the price increase will not be unreasonably denied if the foregoing process is used and justified. Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers.

(d) Adjustments Due to Currency Fluctuations. If the parties agree in a Product Agreement to invoice in a currency other than the local currency for the Manufacturing Site, Patheon will adjust the Price to reflect currency fluctuations. The adjustment will be calculated after all other annual Price adjustments under this Section 4.2 have been made. The adjustment will proportionately reflect the increase or decrease, if any, in the Set Exchange Rate compared to the Set Exchange Rate established for the prior Year or the Initial Set Exchange Rate, as the case may be. An example of the calculation of the price adjustment (for a Canadian Manufacturing Site invoiced in USD) is set forth in Exhibit E.

(e) Tier Pricing (if applicable). The pricing in Schedule B of a Product Agreement is set forth in Annual Volume tiers based upon the Client's volume forecasts under Section 5.1. The Client will be invoiced during the Year for the unit price set forth in the Annual Volume tier based on the [***] forecast provided in [***]. Within [***], Patheon will send Client a reconciliation of the actual volume of Product ordered by the Client during the Year with the pricing tiers. If Client has overpaid during the Year, Patheon will issue a credit to the Client for the amount of the overpayment [***] or will issue payment to the Client for the overpayment [***]. If Client has underpaid during the Year, Patheon will issue an invoice to the Client under Section 5.6 for the amount of the underpayment [***]. If Client disagrees with the reconciliation, the parties will work in good faith to resolve the disagreement amicably. If the parties are unable to resolve the disagreement [***], the matter will be handled under Section 12.1.

(f) For all Price adjustments under this Section 4.2, Patheon will deliver to Client on or before [***] a revised Schedule B to the Product Agreement to be effective for Product delivered on or after the first day of the next Year. If in any Year Patheon would have been entitled to increase the Price based on any of the provisions of this Section 4.2 but Patheon did not exercise its right to do so, then solely at the expiry of the next subsequent Year, Patheon will be entitled to make a cumulative adjustment for the two year period going forward as if it had made adjustments for each of the two Years. Under no circumstance shall Patheon be entitled to make a price adjustment hereunder for a Year by going back past the immediately prior Year (if no such adjustment had been made for such immediately prior Year). It is not the intention of this section for any such adjustments to be applied retroactively.

4.2.1 The Parties acknowledge that Sterile Products are not included in this Agreement.

4.3 Price Adjustments – Current Year Pricing.

During any Year, the Prices set out in Schedule B of a Product Agreement will be adjusted as follows:

Extraordinary Increases or Decreases in Component Costs. If, at any time, market conditions result in Patheon's cost of Components being materially greater than normal forecasted increases, then Patheon will be entitled to an adjustment to the Price for any affected Product to compensate it for the increased Component costs. Changes materially greater than normal forecasted increases will have occurred if: (i) the cost of a Component increases or decreases [***] of the cost for that Component upon which the most recent fee quote was based; or (ii) the aggregate cost for all Components required to manufacture a Product increases or decreases [***] of the total Component costs for the Product upon which the most recent fee quote was based. If Component costs have been previously adjusted to reflect an increase in the cost of one or more Components, the adjustments set out in (i) and (ii) above will operate based on the last cost adjustment for the Components.
For a Price adjustment under this Section 4.3, Patheon will deliver to Client a revised Schedule B to the Product Agreement and budgetary pricing information, adjusted Component costs or other documents reasonably sufficient to demonstrate that a Price adjustment is justified. Patheon will have no obligation to

deliver any supporting documents that are subject to obligations of confidentiality between Patheon and its suppliers. The revised Price will be effective for any Product delivered on or after the first day of the month following Client's receipt of the revised Schedule B to the Product Agreement.

4.4 Adjustments Due to Technical Changes or Regulatory Authority Requirements.

(a) Technical Changes to Requirements. Technical changes requested by Client will only be implemented following a technical and cost review that Patheon will perform and are subject to Client and Patheon reaching agreement on Price changes required because of the amendment. Technical changes requested by Patheon will only be implemented following an assessment by Patheon and the Client regarding the technical changes that may have an effect on certain areas including, but not limited to Regulatory filings, fees, etc. All technical changes requested by Patheon require the written approval of Client, the approval not to be unreasonably withheld. If Client accepts a proposed Price change, the proposed change in the Specifications and the associated scope of work will be implemented at Client's cost. All costs relating to the technical changes, including re-validations of the process, or stability program shall be determined by the parties after good faith discussions, and the Price change will become effective only for those orders of Products that are manufactured under the revised Specifications. In addition, Client agrees to purchase, at Patheon's cost (including all costs incurred by Patheon for the purchase and handling of the Inventory), all Inventory for Firm Orders used under the "old" Specifications and purchased or maintained by Patheon in order to fill Firm Orders or under Section 5.2, if the Inventory can no longer be used under the revised Specifications. Open purchase orders for Components no longer required under any revised Specifications that were placed by Patheon with suppliers in order to fill Firm Orders or under Section 5.2 will be cancelled where possible, and if the orders may not be cancelled without penalty, will be assigned to and satisfied by Client.

(b) Regulatory Changes to Authority Requirements. Regulatory changes to the Specifications requested by Client will be implemented immediately, and will be followed by a good faith effort from both parties to evaluate the cost impact. Regulatory changes to the Manufacturing Site will only be implemented following the written approval of Client, the approval not to be unreasonably withheld. The cost of any such changes shall be agreed to in advance by the parties after good faith discussions.

4.5 Multi-Country Packaging Requirements.

If Client decides to have Patheon perform Manufacturing Services for the Product for countries outside the Territory, then Client will inform Patheon of the packaging requirements for each new country and Patheon will prepare a quotation for consideration by Client of any additional costs for Components (other than Client-Supplied Components) and the change over fees for the Product destined

for each new country. The agreed additional packaging requirements and related packaging costs and change over fees will be set out in a written amendment to this Agreement.

ARTICLE 5
ORDERS, SHIPMENT, INVOICING, PAYMENT

5.1 Orders and Forecasts.

(a) Long Term Forecast. When each Product Agreement is executed, Client will give Patheon a non-binding [***] forecast of Client's volume requirements for the Product for the [***] of the term of the Product Agreement (the "**Long Term Forecast**"). The Long Term Forecast will thereafter be updated annually, [***]. If Patheon is unable to accommodate any portion of the Long Term Forecast, it will notify Client and the parties will agree on any revisions to the forecast.

(b) Rolling [***] Forecast. When each Product Agreement is executed, Client will give Patheon a non-binding [***] forecast of the volume of Product that Client expects to order in the [***] of commercial manufacture of the Product. This forecast will then be updated by Client on or before the [***] on a rolling forward basis. Client will update the forecast forthwith if it determines that the volumes estimated in the most recent forecast have changed by more than [***]. The most recent [***] forecast will prevail.

(c) Firm Orders. On a rolling basis during the term of the Product Agreement, Client will issue an updated [***] forecast on or before the [***]. This forecast will start on [***]. Unless otherwise agreed in the Product Agreement, the first [***] of this updated forecast will be considered binding firm orders. Concurrent with the [***] forecast, Client will issue a new firm written order in the form of a purchase order or otherwise ("**Firm Order**") by Client to purchase and, when accepted by Patheon, for Patheon to manufacture and deliver the agreed quantity of the Products. The Delivery Date will not be less than [***] following the date that the Firm Order is submitted. Firm Orders submitted to Patheon will specify Client's purchase order number, quantities by Product type, monthly delivery schedule, and any other elements necessary to ensure the timely manufacture and shipment of the Products. The quantities of Products ordered in those written orders will be firm and binding on Client and may not be reduced by Client. Further, for [***] of the [***] forecast, Client commits that its Firm Orders for each of those months will be no less than [***], respectively, of the forecasted amounts for [***]. If Client orders less than the agreed volume, the parties will meet to discuss how to smooth production to meet demand. If it is not possible to smooth production to meet forecasted demand, Client will compensate Patheon for not meeting the Firm Order commitment by paying the [***] for the shortfall between what Client actually ordered and its Firm Order commitment as set forth above or as otherwise provided for in the applicable Product Agreement. The forgoing shall be Patheon's sole and exclusive remedy for Client's failure to meet the Firm Order commitment. No amounts shall be payable to Patheon if Client is unable to make the Firm Order commitment because of Force Majeure or because the Product is taken off the market due in response to an action by an Authority or otherwise as required by Applicable Law. Patheon commits to make [***] of the forecasted amounts available to Client, and will reserve [***] of its capacity to meet that commitment. Patheon shall notify Client as soon as possible of impending capacity constraints in relation to Client's forecasts and/or changes in Client's demands.

(d) Acceptance of Firm Order. Patheon will accept Firm Orders by sending an acknowledgement to Client within [***] of its receipt of the Firm Order. The acknowledgement will include, subject to confirmation from the Client, the Delivery Date for the Product ordered. The Delivery Date may be amended by agreement of the parties or as set forth in Section 2.1(f). If Patheon fails to acknowledge receipt of a Firm Order within the [***] period, the Firm Order will be deemed to have been accepted by Patheon.

(e) Cancellation of a Firm Order. Except for [***], if Client cancels a Firm Order, Client will pay Patheon the [***] for the Firm Order. For purposes of this provision, [***] . Patheon will use commercially reasonable efforts to mitigate all costs related to a cancellation of a Firm Order and to deploy its resources to other clients.

(f) On Time Delivery.

(i) Patheon and the Client understand that there may be uncertainties and necessary adjustments in production schedules during the first 6 months of Manufacturing. The parties agree that they will work together closely to expedite deliveries and manage the scheduling of the initial Product launch.

(ii) If, [***], Patheon is unable to deliver the quantity of Product ordered under a Firm Order [***] of the Delivery Date due to an act or omission by Patheon (a "**Late Delivery**"), [***]. Nothing herein shall preclude Client from exercising any other rights it may have under this Agreement in connection with Patheon's failure to timely delivery Product.

(iii) A Late Delivery will not be a material breach of this Agreement by Patheon for the purposes of Section 8.2. If Patheon has [***] Late Deliveries in any [***], the parties will meet as necessary to amicably resolve the reasons for the Late Deliveries. The parties will agree on a delivery improvement plan [***]. If, after the delivery improvement plan is in place, Patheon has [***] Late Deliveries in any [***], Client may exercise its right to terminate this Agreement for cause under Section 8.2(a) without a further opportunity to cure.

(iv) For clarity, a Late Delivery will not include any delay in shipment of Product caused by events outside of Patheon's reasonable control, such as a Force Majeure Event, a delay in delivery of API or Materials (provided that Patheon ordered Materials with sufficient lead time for such Materials to be delivered on a timely basis), a delay in Product release approval from Client, inaccurate Client forecasts, or receipt of non-conforming API or Components supplied by Client.

(g) Zero Volume Forecast. If Client forecasts zero volume for [***] (the "**Zero Forecast Period"**), then Patheon will have the option, at its sole discretion, to provide a [***] notice to Client of Patheon's intention to terminate the Product Agreement on a stated day within the Zero Forecast Period. Client thereafter will have [***] to either (i) withdraw the zero forecast and re-submit a reasonable volume forecast, or (ii) negotiate other terms and conditions on which the Product Agreement will remain in effect. Otherwise, Patheon will have the right to terminate the Product Agreement at the end of the [***] notice period.

5.2 Reliance by Patheon.

(a) Client understands and acknowledges that Patheon will rely on the Firm Orders and rolling forecasts submitted under Sections 5.1(a) (b) and (c) in ordering the Components (other than Client-Supplied Components) required to meet the Firm Orders. In addition, Client understands that to ensure an orderly supply of the Components, Patheon may want to purchase the Components in sufficient volumes to meet the production requirements for Products during part or all of the forecasted periods referred to in Section 5.1(a) or to meet the production requirements of any longer period agreed to by Patheon and Client. Accordingly, Client authorizes Patheon to purchase Components to satisfy the Manufacturing Services requirements for Products [***] contemplated in the most recent forecast given by Client under Section 5.1(a). Patheon may make other purchases of Components to meet Manufacturing Services requirements for longer periods if agreed to in writing by the parties. The Client will give Patheon written authorization to order Components for any launch quantities of Product requested by Client which will be considered a Firm Order when accepted by Patheon.

(b) Client will reimburse Patheon for the cost of Components ordered by Patheon under Firm Orders or under Section 5.2(a) that are not included in finished Products manufactured for Client within six months after the forecasted month for which the purchases have been made (or for a longer period as the parties may agree) or if the Components have expired or are rendered obsolete due to changes in artwork or applicable regulations during the period (collectively, "**Obsolete Stock**"). This reimbursement will include Patheon's cost to purchase (plus a [***] handling fee) and destroy the Obsolete Stock. If any non-expired Components are used in Products subsequently manufactured for Client or in third party products manufactured by Patheon, Client will receive credit for any costs of those Components previously paid to Patheon by Client.

(c) If Client fails to take possession or arrange for the destruction of non-expired Components (whose purchase was authorized by Client per Section 5.2 (a)) [***] or, in the case of the delivery of conforming finished Product not accepted by Client [***], Client will pay Patheon [***] per pallet, per month thereafter for storing the Components or finished Product. During the parties' normal quarterly reviews, Patheon will detail all potential storage costs. To the extent applicable, storage fees for Components or Product which contain controlled substances or require refrigeration will be charged at [***]per pallet per month. Storage fees are subject to a one pallet minimum charge per month. Patheon may ship finished Product held by it longer than [***] to the Client at Client's expense on [***] written notice to the Client.

5.3 Minimum Orders.

Client may only order Manufacturing Services for batches of Products at or greater than the Minimum Order Quantities as set out in Schedule B to a Product Agreement.

5.4 Delivery and Shipping.

Upon acceptance from Client's Quality Assurance Department, the Product will be delivered to Client after it has been manufactured and released to the Client by Patheon and released by Client; provided however that such acceptance release by Client shall be within [***] of receipt of all required batch documentation and release to ship by Patheon. Delivery of Products will be made EXW (Incoterms 2010) Patheon's shipping point unless otherwise agreed in a Product Agreement. Risk of loss or of damage to Products will remain with Patheon until Patheon loads the Products onto the carrier's vehicle for shipment at the shipping point at which time risk of loss or damage will transfer to Client.

Patheon will, in accordance with Client's instructions and as agent for Client, at Client's risk, (i) arrange for shipping to be paid by Client and (ii) at Client's risk and expense, obtain any export license or other official authorization necessary to export the Products. Client will arrange for insurance and will select the freight carrier used by Patheon to ship Products and may monitor Patheon's shipping and freight practices as they pertain to this Agreement. Products will be transported in accordance with the Specifications.

5.5 Invoices and Payment.

Invoices will be sent by email to the email address given by Client to Patheon in writing. Invoices will be issued when the Product is manufactured and released by Patheon and Client. Patheon will also give Client an invoice covering any Inventory or Components which are to be purchased by Client under Section 5.2 of this Agreement. Each invoice will, to the extent applicable, identify Client's Manufacturing Services purchase order number, Product numbers, names and quantities, unit price, freight charges, and the total amount to be paid by Client. Client will pay all invoices within [***] of the date of Client's receipt of an undisputed invoice. If any portion of an invoice is disputed, the Client will pay Patheon for the undisputed amount and the parties will use good faith efforts to reconcile the disputed amount as soon as practicable. Interest on undisputed past due accounts will accrue at [***] per month which is equal to an annual rate of [***].

ARTICLE 6
PRODUCT CLAIMS AND RECALLS

6.1 Product Claims.

(a) Product Claims. Client has the right to reject any portion or all of any shipment of Products that deviates from the Specifications, cGMPs, or Applicable Laws without invalidating any remainder of the shipment. Client will inspect the Products manufactured by Patheon upon receipt and will give Patheon written notice (a "**Deficiency Notice**") of all claims for Products that deviate from the Specifications, cGMPs, or Applicable Laws within [***] after Client's receipt thereof (or, in the case of any defects not reasonably susceptible to discovery upon receipt of the Product, within [***] after discovery by Client, but not after the expiration date of the Product). Should Client fail to give Patheon the Deficiency Notice within the applicable [***] period, then the delivery will be deemed to have been accepted by Client on the [***] after delivery or discovery, as applicable. Patheon will have no liability for any deviations for which it has not received notice within the applicable [***] period.

(b) Determination of Deficiency. Upon receipt of a Deficiency Notice, Patheon will have [***] to advise Client by notice in writing that it disagrees with the contents of the Deficiency Notice. If Client and Patheon fail to agree within ten days after Patheon's notice to Client as to whether any Products identified in the Deficiency Notice deviate from the Specifications, cGMPs, or Applicable Laws, then the parties will mutually select an independent qualified investigator and/or laboratory to evaluate if the Products deviate from the Specifications, cGMPs, or Applicable Laws. This evaluation will be binding on the parties. If the evaluation certifies that any Products deviate from the Specifications, cGMPs, or Applicable Laws, Client may reject those Products in the manner contemplated in this Section 6.1 and Patheon will be responsible

for the cost of the evaluation. If the evaluation does not so certify for any of the Products, then Client will be deemed to have accepted delivery of the Products on [***] after delivery (or, in the case of any defects not reasonably susceptible to discovery upon receipt of the Product, on [***] after discovery thereof by Client, but not after the expiration date of the Product) and Client will be responsible for the cost of the evaluation.

(c) Shortages and Price Disputes. Claims for shortages in the amount of Products shipped by Patheon or a Price dispute will be dealt with by reasonable agreement of the parties. Any claim for a shortage or a Price dispute will be deemed waived if it has not been presented within [***] of the date of a compliant invoice meeting the requirements of this Agreement.

(d) Product Rejection for Finished Product Specification Failure. Internal process specifications will be defined and agreed upon. If after a full investigation as set forth in Section 6.1(b), it is determined that Patheon manufactured Product in accordance with the agreed upon in-process specifications, cGMP, the batch production record, Patheon's standard operating procedures for manufacturing and the other requirements of the Agreement and the applicable Product Agreement, and a batch or portion of batch of Product does not meet a finished Product Specification, Client will pay Patheon [***] for the non-conforming Product. Patheon will be responsible for the materials and Client will be responsible for the API. The API in the non-conforming Product will be included in the "Quantity Converted" for purposes of calculating the "Actual Annual Yield" under Section 2.2(a). If it is determined that the Product failure is due to error on Patheon's part, Patheon will pay for product disposal, provide a certificate of destruction to the Client, and the API in the non-conforming Product will be excluded from the "Quantity Converted" for purposes of calculating the "Actual Annual Yield" under Section 2.2(a).

6.2 Product Recalls and Returns.

(a) Records and Notice. Patheon and Client will each maintain records necessary to permit a Recall of any Products delivered to Client or customers of Client. Each party will promptly notify the other by telephone (to be confirmed in writing) of any information which might affect the marketability, safety or effectiveness of the Products or which might result in the Recall or seizure of the Products. Upon receiving this notice or upon this discovery, each party will stop making any further shipments of any affected Products in its possession or control until a decision has been made whether a Recall or some other corrective action is necessary. The decision to initiate a Recall or to take some other corrective action, if any, will be made and implemented by Client. "**Recall**" will mean any action (i) by Client to recover title to or possession of quantities of the Products sold or shipped to third parties (including, without limitation, the voluntary withdrawal of Products from the market); or (ii) by any Authorities to detain or destroy any of the Products. Recall will also include any action by either party to refrain from selling or shipping quantities of the Products to third parties which would have been subject to a Recall if sold or shipped.

(b) Recalls. If (i) any Authority issues a directive, order or, following the issuance of a safety warning or alert about a Product, a written request that any Product be Recalled, (ii) a court of competent jurisdiction orders a Recall, or (iii) Client determines that any Product should be Recalled or that a "Dear Doctor" letter is required relating the restrictions on the use of any Product, Patheon will co-operate as reasonably required by Client, having regard to all applicable laws and regulations.

(c) Product Returns. Client will have the responsibility for handling customer returns of the Products. Patheon will give Client any assistance that Client may reasonably require to handle the returns.

6.3 Patheon's Responsibility for Defective and Recalled Products.

(a) Defective Product. If Client rejects Products under Section 6.1 and the deviation is determined to have arisen from Patheon's failure to provide the Manufacturing Services in accordance with the Specifications, cGMPs, Applicable Laws, or the other requirements of this Agreement or the applicable Product Agreement) Patheon will credit Client's account for Patheon's invoice price for the defective Products. If Client previously paid for the defective Products, Patheon will promptly, at Client's election, either: (i) refund the invoice price for the defective Products; (ii) offset the amount paid against other amounts due to Patheon hereunder; or (iii) replace the Products with conforming Products without Client being liable for payment therefore under Section 3.1, contingent upon the receipt from Client of all Active Materials and Client-Supplied Components required for the manufacture of the replacement Products. For greater clarity, Patheon's responsibility for any loss of Active Materials in defective Product will be captured and calculated in the Active Materials Yield under Section 2.2. Patheon shall promptly reimburse Client for all costs related to the production and shipment of the Client-Supplied Components to Patheon related to the defective Product.

(b) Recalled Product. If a Recall or return results from, or arises out of, a failure by Patheon to provide Product that conforms with the Specifications, cGMPs, Applicable Laws or the other requirements of this Agreement or the applicable Product Agreement, in addition to the amounts described under Section 6.3(a), Patheon will also be responsible for the documented out-of-pocket expenses of the Recall or return. For greater clarity, Patheon's responsibility for any loss of Active Materials in Recalled Product will be captured and calculated in the Active Materials Yield under Section 2.2. In all other circumstances, Recalls, returns, or other corrective actions will be made at Client's cost and expense.

(c) Replacement Product. If (i) Client rejects Product under Section 6.3(a) and Patheon or (ii) (A) an independent laboratory pursuant to Section 6.1 determines that or (B) Product is recalled because the Product manufactured and released by Patheon deviates from the Specifications, GMPs, Applicable Laws, or any other requirement of this Agreement or the applicable Product Agreement, Client shall have the right to avail itself of the remedies set forth in Section 6.3(a) above.

(d) Except as set forth in Sections 6.3(a) and (b) above, Patheon will not be liable to Client nor have any responsibility to Client for any deficiencies in, or other liabilities associated with, any Product manufactured by it, (collectively, "**Product Claims**"). For greater certainty, Patheon will have no obligation for any Product Claims to the extent the Product Claim (i) is caused by deficiencies in the Specifications, the safety, efficacy, or marketability of the Products or any distribution thereof, (ii) results from a defect in a Component that is not reasonably discoverable by Patheon using the test methods set forth in the Specifications, (iii) results from a defect in the Active Materials, Client-Supplied Components or Components supplied by a Client designated additional source that is not reasonably discoverable by Patheon using the test methods set forth in the Specifications, (iv) is caused by actions of third parties occurring after the Product is shipped by Patheon under Section 5.4, (v) is due to packaging design or labelling defects or omissions for which Patheon has no responsibility, (vi) is due to any unascertainable reason despite Patheon having performed the Manufacturing Services in accordance with the Specifications, cGMP's, and Applicable Laws, or (vii) is due to any other breach by Client of its obligations under this Agreement.

6.4 Disposition of Defective or Recalled Products.

Client will not dispose of any damaged, defective, returned, or Recalled Products for which it intends to assert a claim against Patheon without Patheon's prior written authorization to do so. Alternatively, Patheon may instruct Client to return the Products to Patheon. Patheon will bear the cost of disposition for any damaged, defective, returned or Recalled Products for which it bears responsibility under Section 6.3. In all other circumstances, Client will bear the cost of disposition, including all applicable fees for Manufacturing Services, for any damaged, defective, returned, or Recalled Products.

6.5 Healthcare Provider or Patient Questions and Complaints.

Client will have the sole responsibility for responding to questions and complaints from its customers. Questions or complaints received by Patheon from Client's customers, healthcare providers or patients will be promptly referred to Client. Patheon will co-operate as reasonably required to allow Client to determine the cause of and resolve any questions and complaints. This assistance will include follow-up investigations, including testing. In addition, Patheon will give Client all agreed upon information that will enable Client to respond properly to questions or complaints about the Products as set forth in the Quality Agreement. Unless it is determined that the cause of the complaint resulted from a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws, all costs incurred under this Section 6.5 will be borne by Client.

6.6 Sole Remedy.

Except for the indemnity set forth in Section 10.3 [***] and subject to the limitations set forth in Sections 10.1 and 10.2, the remedies described in this Article 6, along with any termination rights permitted under this Agreement, will be Client's sole remedy for any failure by Patheon to provide the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws.

ARTICLE 7

.

CO-OPERATION

7.1 Quarterly Review.

Each party will forthwith upon execution of this Agreement appoint one of its employees to be a relationship manager responsible for liaison between the parties. The relationship managers will meet not less than quarterly to review the current status of the business relationship and manage any issues that have arisen. At each Quarterly Review, Patheon should prepare and provide Client data and reports relating to manufacturing, yield performance, analytical results, inventory, forecasts, and any other matters reasonably requested by Client. Also, Patheon should provide all of the past and on-going quality issues specifically related to Client's Products including Out Of Trend (OOT), Out Of specifications (OOS), deviation investigations and reports.

7.2 Governmental Agencies.

Subject to Section 7.8, except as otherwise required by Applicable Law, Client (or its designated representatives) shall be the sole communicator with any Authority, including but not limited to governmental agencies, such as the FDA and EMA, responsible for granting regulatory approval for the Products, regarding the Products. Except as otherwise required by Applicable Law or otherwise permitted in this Section 7, Patheon shall not initiate contact with any Authority regarding the Products or respond to any inquiry or communication from any Authority regarding the Products without Client's prior written approval. If Client is required to submit to an Authority any information concerning the Products or any services provided hereunder, Patheon will provide Client copies of such documentation, data and other information as shall be necessary or reasonably desirable for such submission to the Authorities and such other information in such form as Client may reasonably request. Patheon shall also cooperate and consult as reasonably requested by Client and/or required by the Authorities for development of additional data or performance of studies concerning the Product. Client shall pay Patheon's reasonable costs and fees for performance under this section. Patheon shall also provide, if required by the Authorities, information concerning its laboratory, manufacturing, quality control procedures and CMC matters with respect to its activities under this Agreement, including any Product Agreement. Patheon shall provide Client all documentation, data and information referred to in this Section 7.2 reasonably in advance of their required submission to allow for Client's review and comment. Patheon shall endeavor in good faith to satisfactorily resolve/incorporate all Client comments prior to submission.

7.3 Records and Accounting by Patheon.

Patheon will keep records of the manufacture, testing, and shipping of the Products, and retain samples of the Products as are necessary to comply with manufacturing regulatory requirements applicable to Patheon, as well as to assist with resolving Product complaints and other similar investigations. Further information regarding the Records and Accounting by Patheon is set forth in the parties' Quality Agreement.

7.4 Inspection.

Client may inspect Patheon reports and records relating to this Agreement during normal business hours and with reasonable advance notice, but a Patheon representative must be present during the inspection.

7.5 Access.

Patheon will give Client reasonable access at agreed times to the areas of the Manufacturing Site in which the Products are manufactured, stored, handled, or shipped to permit Client to verify that the Manufacturing Services are being performed in accordance with the Specifications, cGMPs, and Applicable Laws, including reasonable access to the appropriate manufacturing areas while Client products are being manufactured. But, with the exception of "for-cause" audits, Client will be limited each Year to [***] cGMP-type audit, lasting no more than [***], and involving no more than [***]. Client may request additional cGMP-type audits, additional audit days, or the participation of additional auditors subject to payment to Patheon of [***] for each additional audit day and [***] per audit day for each additional auditor. The right of access set forth in Sections 7.4 and 7.5 will not include a right to access or inspect Patheon's financial records.

7.6 Notification of Regulatory Inspections.

Patheon will notify Client as soon as possible but no more than [***] of receipt of any inspections by any Authority specifically involving the Products or otherwise relating to quality matters at the Manufacturing Site or the other facilities in which the Manufacturing Services are performed. Patheon will also notify Client of receipt of any form 483's or warning letters or any other significant regulatory action or communication from any Authority that relate to the Products or the facility in which the Manufacturing Services are performed or could otherwise reasonably be expected to impact Patheon's ability to perform hereunder, and provide Client with a copy of such FDA Form 483s, warning letter or any other documents relating to significant regulatory action or communication from any Authority. In connection with any response by Patheon to such Authority related to Products, Patheon shall provide Client all relevant documentation, data and information reasonably in advance of the required submission to allow for Client's review and comment. Patheon shall endeavor in good faith to satisfactorily resolve/incorporate all Client comments prior to submission

7.7 Reports.

Patheon will supply [***] all Product data in its control, including release test results, change controls, complaint test results, and all investigations (in manufacturing, testing, and storage), that Client reasonably requires in order to complete any filing under any applicable regulatory regime, including any Annual Report that Client is required to file with the FDA. Any additional report requested by Client beyond the scope of cGMPs and customary FDA requirements will be subject to an additional fee to be agreed upon between Patheon and the Client.

7.8 Regulatory Filings.

(a) Regulatory Authority. Client will have the sole responsibility for filing all documents with all Regulatory Authorities and taking any other actions that may be required for the receipt and/or maintenance of Regulatory Authority approval for the commercial manufacture of the Products. Patheon will assist Client, to the extent consistent with Patheon's obligations under this Agreement, to obtain Regulatory Authority approval for the commercial manufacture of all Products as quickly as reasonably possible.

(b) Verification of Data. Prior to filing any documents with any Regulatory Authority that incorporate data generated by Patheon, Client will give Patheon a copy of the relevant portions of the documents incorporating this data to give Patheon the opportunity to verify the accuracy and regulatory validity of those documents as they relate to Patheon generated data. Patheon will promptly review the proposed submission and in no event shall take more than [***] (or such shorter period as required to

meet the submission date for the relevant document) to perform this review and the parties may agree to a shorter time for the review as needed.

(c)Verification of CMC. Prior to filing with any Regulatory Authority any documentation which is or is equivalent to the FDA's Chemistry and Manufacturing Controls (all such documentation herein referred to as "**CMC**") related to any Marketing Authorization, such as a New Drug Application or Abbreviated New Drug Application, Client will give Patheon a redacted copy of the Drug-Product portion of the CMC as well as all supporting documents which have been relied upon to prepare the CMC. This disclosure will permit Patheon to verify that the CMC accurately describes the work that Patheon has performed and the manufacturing processes that Patheon will perform under this Agreement. Patheon requires [***] to perform this review but the parties may agree to a shorter time for the review as needed. Client will give Patheon copies of all FDA filings at the time of submission which contain CMC information regarding the Product.

(d) Deficiencies. If, in Patheon's sole discretion, acting reasonably, Patheon determines that any of the information given by Client under clauses (b) and (c) above is inaccurate or deficient in any manner whatsoever (the "**Deficiencies**"), Patheon will notify Client in writing of the Deficiencies. The parties will work together to have the Deficiencies resolved prior to any pre-approval inspection.

(e) Client Responsibility. For clarity, the parties agree that in reviewing the documents referred to in clause (b) above, Patheon's role will be limited to verifying the accuracy of the description of the work undertaken or to be undertaken by Patheon. Subject to the foregoing, Patheon will not assume any responsibility for the accuracy of any application for receipt of an approval by a Regulatory Authority. The Client is solely responsible for the preparation and filing of the application for approval by the Regulatory Authority and any relevant costs will be borne by the Client.

7.9 Inspection by Regulatory Authorities.

If Client does not give Patheon the documents requested under clause 7.7(b) above within the time specified and if Patheon reasonably believes that Patheon's standing with a Regulatory Authority may be jeopardized, Patheon may, in its sole discretion, delay or postpone any inspection by the Regulatory Authority until Patheon has reviewed the requested documents and is satisfied with their contents.

ARTICLE 8
TERM AND TERMINATION

8.1 Initial Term.

This Agreement will become effective as of the Effective Date and will continue until December 31, 2021 (the "**Initial Term**"), unless terminated earlier by one of the parties in accordance herewith. This Agreement will automatically renew after the Initial Term for successive terms of two Years each if there is a Product Agreement in effect, unless either party gives written notice to the other party of its intention to terminate this Agreement at least 24 months prior to the end of the then current term. In any event, the legal terms and conditions of this Agreement will continue to govern any Product Agreement in effect as provided in Section 1.2. Each Product Agreement will have an initial term of five Years from the start of commercial manufacture at the Manufacturing Site for the Product unless the

parties agree to a different number of Years in the applicable Product Agreement (each, an "**Initial Product Term**"). Product Agreements will automatically renew after the Initial Product Term for successive terms of two Years each unless either party gives written notice to the other party of its intention to terminate the Product Agreement at least 24 months prior to the end of the then current term.

8.2 Termination for Cause.

(a) Either party at its sole option may terminate this Agreement or a Product Agreement upon written notice where the other party has failed to remedy a material breach of any of its representations, warranties, or other obligations under this Agreement or the Product Agreement and in the case of curable material breaches within 60 days following receipt of a written notice (the "**Remediation Period**") of the breach that expressly states that it is a notice under this Section 8.2(a) (a "**Breach Notice**"). The aggrieved party's right to terminate this Agreement or a Product Agreement under this Section 8.2(a) may only be exercised for a period of 60 days following the expiry of the Remediation Period in the case of remediable breaches (where the breach has not been remedied) and if the termination right in connection with such remediable material breach is not exercised during this period then the aggrieved party will be deemed to have waived the breach of the representation, warranty, or obligation described in the Breach Notice.

(b) Either party at its sole option may immediately terminate this Agreement or a Product Agreement upon written notice, but without prior advance notice, to the other party if: (i) the other party is declared insolvent or bankrupt by a court of competent jurisdiction; (ii) a voluntary petition of bankruptcy is filed in any court of competent jurisdiction by the other party; or (iii) this Agreement or a Product Agreement is assigned by the other party for the benefit of creditors.

(c) Client may terminate a Product Agreement upon 30 days' prior written notice if any Authority takes any action, or raises any objection, that prevents Client from researching, developing, importing, exporting, purchasing, selling or otherwise commercializing the Product (an "**Authority Action**"). But if this occurs, Client must still fulfill all of its obligations under Section 8.4 below and under any Capital Equipment Agreement regarding the Product.

(d) Either party may terminate this Agreement or a Product Agreement upon six months' prior written notice if the other party assigns under Section 13.6 any of its rights under this Agreement or a Product Agreement to an assignee that, in the opinion of the non-assigning party acting reasonably, is (i) not a credit worthy substitute for the other party or (ii) a Competitor of the non-assigning party.

8.3 Product Discontinuation.

Client will give at least [***] advance notice (or such shorter period if required pursuant to an Authority Action) if it intends to no longer order Manufacturing Services for a Product due to this Product's discontinuance in the market.

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8.4 Obligations on Termination.

If a Product Agreement is completed, expires, or is terminated in whole or in part for any reason, then:

(a) Client will take delivery of and pay for all undelivered Products that are manufactured and/or packaged under a Firm Order, at the price in effect at the time the Firm Order was placed;

(b) Client will purchase, at Patheon's cost plus [***] handling fee, the Inventory applicable to the Products which was purchased, produced or maintained by Patheon in contemplation of filling Firm Orders or in accordance with Section 5.2 prior to notice of termination being given; provided that Patheon will make commercially reasonable efforts to mitigate any costs payable by Client in connection therewith, which may include canceling any pending orders for such Components, returning or selling items in the Inventory back to its supplier(s) if possible, or otherwise utilizing such Inventory or Components with other Patheon clients or otherwise in Patheon's business;

(c) Client will satisfy the purchase price payable under Patheon's orders with suppliers of Components, if the orders were made by Patheon in reliance on Firm Orders or in accordance with Section 5.2, and thereafter Client will have sole right, title and interest in and to such Components;

(d) Client acknowledges that no Patheon Competitor will be permitted access to the Manufacturing Site;

(e) Client will make commercially reasonable efforts, at its own expense, to remove from Patheon site(s), [***], all unused Active Material and Client-Supplied Components, all applicable Inventory and Materials (whether current or obsolete), supplies, undelivered Product, chattels, equipment or other moveable property owned by Client, related to the Agreement and located at a Patheon site or that is otherwise under Patheon's care and control ("**Client Property**"). If Client fails to remove the Client Property [***] following the completion, termination, or expiration of the Product Agreement, Client will pay Patheon [***] per pallet, per month, one pallet minimum (except, if applicable, Client will pay [***] per pallet, per month, one pallet minimum, for any of the Client Property that contains controlled substances, requires refrigeration or other special storage requirements) thereafter for storing the Client Property and will assume any third party storage charges invoiced to Patheon regarding the Client Property; provided that no such charges shall be applicable and payable by Client if Client notifies Patheon to destroy/dispose of such Client Property. Patheon will invoice Client for the storage charges as set forth in Section 5.5 of this Agreement;

(f) Pursuant to a reasonable written request from Client to Patheon, Patheon shall transfer to Client and/or its designee any and all Client Intellectual Property in Patheon's possession and shall provide to Client and/or its designee Patheon Intellectual Property, so as to permit Client and/or its designee(s) to produce/manufacture Products with such technical assistance being provided in accordance with a plan provided to Patheon by Client. To the extent transferable, Patheon shall also transfer any license(s) obtained specifically for the production/manufacture of Products under this Agreement. Patheon hereby grants to Client [***] any and all Patheon Intellectual Property to make, have made, use, offer for sale, sell, and import Products, which license shall survive termination of this Agreement. However, no Competitor of Patheon in the business of contract development or manufacture of drug products will be permitted to have access to Patheon's manufacturing site. The third party manufacturer will be required to sign a customary and appropriate confidentiality agreement with Patheon concerning the nondisclosure of Patheon confidential information that may be involved in the transfer;

(g) Except to the extent necessary to complete performance pursuant to subsection (f) or to exercise rights that survive the termination of this Agreement, each party as a receiving party shall deliver to the disclosing party such disclosing party's Confidential Information in the receiving party's possession or control. Notwithstanding anything in this Agreement that may be to the contrary, Client (and its designees) may continue to retain and use Patheon Confidential Information that is required to maintain marketing approval for a Product and/or is useful to production/manufacture of the Product;

(h) Promptly following any notice of termination of expiration, Patheon will update and confirm the technical information and specifications for the Product as set forth in the Specifications (Schedule A), Stability Testing protocols and procedures (Schedule C) and the Quality Agreement (Exhibit B) as applicable, to the extent required to reflect any needed changes to manufacturing and validation methods;

(i) Each party will continue to comply with their obligations under Applicable Law which survive termination of this Agreement;

Any termination or expiration of this Agreement or a Product Agreement will not affect any outstanding obligations or payments due prior to the termination or expiration, nor will it prejudice any other remedies that the parties may have under this Agreement or a Product Agreement or any related Capital Equipment Agreement. For greater certainty, termination of this Agreement or of a Product Agreement for any reason will not affect the obligations and responsibilities of the parties under Articles 10, 11, 12 and 13 and Sections 1.3, 1.5, 1.6, 1.7, 6.2, 6.3, 6.4, 6.5, 6.6, 7.2, 7.3, 7.4, 7.5, 7.6, 7.8, and 8.4, all of which survive any termination.

ARTICLE 9
REPRESENTATIONS, WARRANTIES AND COVENANTS

9.1 Authority.

Each party covenants, represents, and warrants that it has the full right and authority to enter into this Agreement and that it is not aware of any impediment that would inhibit its ability to perform its obligations hereunder.

9.2 Client Warranties.

Client covenants, represents, and warrants that:

(a) Non-Infringement.

(i) the Specifications for each of the Products are its or its Affiliate's property and that Client may lawfully disclose the Specifications to Patheon;

(ii) any Client Intellectual Property, used by Patheon in performing the Manufacturing Services according to the Specifications (A) is Client's or its Affiliate's unencumbered property, (B) may be lawfully used as directed by Client, and (C) to the knowledge of Client does not infringe and will not infringe any Third Party Rights;

(iii) the performance of the Manufacturing Services by Patheon for any Product under this Agreement or any Product Agreement or the use or other disposition of any Product by Patheon as may be required to perform its obligations under this Agreement or under any Product Agreement, to the knowledge of Client, does not and will not infringe any Third Party Rights;

(iv) there are no actions or other legal proceedings against Client, concerning the infringement of Third Party Rights related to any of the Specifications, or any of the Active Materials and the Components, or the sale, use, or other disposition of any Product made in accordance with the Specifications;

(b) Quality and Compliance.

(i) the Specifications for all Products conform to all applicable cGMPs and Applicable Laws;

(ii) the Products, if labelled and manufactured in accordance with the Specifications and in compliance with applicable cGMPs and Applicable Laws may be lawfully sold and distributed in every jurisdiction in which Client markets the Products; and

(iii) on the date of shipment, the API will conform to the specifications for the API that Client has given to Patheon and that the API will be adequately contained, packaged, and labelled and will conform to the affirmations of fact on the container.

9.3 Patheon Warranties.

Patheon covenants, represents, and warrants that:

(a) it will perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws;

(b) it has or shall have and shall maintain all necessary licences, permits, and approvals required by any Regulatory Authority for the manufacture of the Product;

(c) it has disclosed and will disclose to Client all warnings or other notices from any applicable Regulatory Authority it has received relating to its Manufacturing Site to the extent that such notice or warning would affect Patheon's ability to perform the Manufacturing Services in accordance with this Agreement;

(d) it shall not at any time without Client's prior written consent:

(i) make any changes to the manufacturing, packaging, testing, or storage of the Product; or

(ii) knowingly take any actions which would likely affect the validation status or quantity of the Product

(e) any Patheon Intellectual Property used by Patheon to perform the Manufacturing Services (i) is Patheon's or its Affiliate's unencumbered property, (ii) may be lawfully used by Patheon, and (iii) does not knowingly infringe and will not knowingly infringe any Third Party Rights;

(f) the Product when delivered will be in compliance with the certificate of analysis provided by Patheon to Client with respect thereto;

(g) all right, title and interest in the Product will be transferred to Client free of any and all liens, security interests or other encumbrances (provided however, Client has provided all API and Client Supplied Components to Patheon free of any and all liens, security interests or other encumbrances; and

(h) the Manufacturing Services and other work performed hereunder will be performed in a professional, expeditious and workmanlike manner, consistent with industry standards.

9.4 Debarred Persons.

Patheon covenants that it will not in the performance of its obligations under this Agreement use the services of any person debarred or suspended under 21 U.S.C. §335(a) or (b). Patheon represents that it does not currently have, and covenants that it will not hire, as an officer or an employee any person who has been convicted of a felony under the laws of the United States for conduct relating to the regulation of any drug product under the *Federal Food, Drug, and Cosmetic Act* (United States).

9.5 Permits.

Client will be solely responsible for obtaining or maintaining, on a timely basis, any permits or other regulatory approvals for the Products or the Specifications, including, without limitation, all marketing and post-marketing approvals.

Patheon will maintain at all relevant times all governmental permits, licenses, approval, and authorities required to enable it to lawfully and properly perform the Manufacturing Services.

9.6 No Warranty.

EACH PARTY HERETO MAKES NO REPRESENTATION OR WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, BY FACT OR LAW, OTHER THAN THOSE EXPRESSLY SET FORTH IN THIS AGREEMENT, INCLUDING ANY IMPLIED REPRESENTATION OR WARRANTY WITH RESPECT TO (I) MERCHANTABILITY, NON-INFRINGEMENT, SUITABILITY OR FITNESS FOR A PARTICULAR PURPOSE, (II) THE LIKELIHOOD OF SUCCESS OF ANY APPLICATION FOR MARKETING AUTHORIZATION RELATING TO ANY PRODUCTS CURRENTLY IN DEVELOPMENT OR FOR WHICH MARKETING AUTHORIZATION HAS NOT YET BEEN GRANTED EITHER IN THE U.S. OR IN ANY OTHER COUNTRY, OR (III) THE PROBABLE SUCCESS OR PROFITABILITY OF ANY PRODUCTS AFTER THE EFFECTIVE DATE.

ARTICLE 10
REMEDIES AND INDEMNITIES

10.1 Consequential Damages.

Except in connection with [***] provisions of this Agreement (all the foregoing the "**Exceptions**"), under no other circumstances whatsoever will either party be liable to the other in contract, tort, negligence, breach of statutory duty, or otherwise for (i) any (direct or indirect) loss of profits, of production, of anticipated savings, of business, or goodwill or (ii) for any other liability, damage, costs, or expense of any kind incurred by the other party of an indirect or consequential nature, regardless of any notice of the possibility of these damages.

10.2 Limitation of Liability.

(a) Defective or Recalled Product. Other than in the case of the Exceptions, Patheon's maximum aggregate liability to Client for any obligation to (i) refund, offset or replace any defective Product under Section 6.3(a) or (ii) replace any recalled Products under Section 6.3(b), will not [***]. This Section 10.2(a) will not be subject to Section 10.2(c).

(b) Active Materials. Except (i) as expressly set forth in Section 2.2, (ii) in connection with the Exceptions, (iii) [***] and (iv) as otherwise provided under this Agreement, Patheon will not be responsible for any loss or damage to the Active Materials and Patheon's maximum responsibility for loss or damage to the Active Materials will not exceed the Maximum Credit Value set forth in Schedule D of a Product Agreement.

(c) Maximum Liability. Other than in the case of the Exceptions, [***] and as provided under Section 10.2(a) above, Patheon's maximum liability to Client under this Agreement or any Product Agreement for any reason whatsoever will not exceed on a per Product basis [***].

(d) Nothing in this Agreement is intended to limit either party's liability for death or personal injury caused by its negligence or fraudulent misrepresentation.

10.3 Patheon Indemnity.

(a) Patheon agrees to defend and indemnify and hold harmless Client, its officers, employees, Affiliates and agents against all losses, damages, fines, penalties, costs, expenses (including reasonable attorneys' fees and court costs), claims, suits, proceedings, demands, judgments and liability to, from and in favour of third parties (other than Affiliates) (all the foregoing, "**Third-Party Claims**") resulting from, or relating to (i) any claim that is the result of a failure by Patheon to perform its obligations under this Agreement, including that the Manufacturing Services were not performed in accordance with the Specifications, cGMPs, and Applicable Laws and the other requirements of this Agreement and the applicable Product Agreement, (ii) the gross negligence or willful misconduct of Patheon or any of its personnel, representatives, Affiliates or subcontractors or, (iii) any claim of infringement or alleged infringement of any Third Party Rights regarding the use of Patheon Intellectual Property pursuant to this Agreement (but excluding any Client Intellectual Property included or utilized in connection therewith) except to the extent that such Third Party Claims are due to the negligence or wrongful act(s) of Client, its officers, employees, agents, or Affiliates.

(b) If a Third-Party Claim occurs for which indemnification is sought under the foregoing, Client will: (a) promptly notify Patheon of the Third-Party Claim; (b) use commercially reasonable efforts to mitigate the effects of the claim; (c) reasonably cooperate with Patheon in the defense of the Third-Party Claim (at Patheon's sole cost and expense); and (d) permit Patheon to control the defense and settlement of the Third-Party Claim, all at Patheon's cost and expense. Client and the other indemnitees may participate in the defense and settlement of any Third-Party Claim using counsel of its own choice at its own expense. Patheon shall not settle any Third-Party Claim in a manner that adversely affects the rights of the Client or any other indemnitee without the Client's or such other indemnitee's prior written consent, which shall not be unreasonably withheld or delayed. The Client's or any other indemnitee's failure to perform any obligations under this Section shall not relieve Patheon of its obligations hereunder, except to the extent that Patheon can demonstrate that it has been materially prejudiced as a result of such failure.

10.4 Client Indemnity.

(a) Client agrees to defend and indemnify and hold harmless Patheon, its officers, employees, and agents against all Third-Party Claims resulting from, or relating to any claim of infringement or alleged infringement of any Third Party Rights in the Products, or any portion thereof (but excluding any Patheon Intellectual Property included or utilized in connection therewith), or any claim that is the result of a breach of this Agreement by Client, including, without limitation, any representation or warranty contained herein, except to the extent that the Third-Party Claims are due to the negligence or wrongful act(s) of Patheon, its officers, employees, Affiliates or agents.

(b) If a Third-Party Claim occurs for which indemnification is sought under the foregoing, Patheon will: (a) promptly notify Client of the Third-Party Claim; (b) use commercially reasonable efforts to mitigate the effects of the claim; (c) reasonably cooperate with Client in the defense of the Third-Party Claim (at Client's sole cost and expense); and (d) permit Client to control the defense and settlement of the Third-Party Claim, all at Client's cost and expense. Patheon and the other indemnitees may participate in the defense and settlement of any Third-Party Claim using counsel of its own choice at its own expense. Client shall not settle any Third-Party Claim in a manner that adversely affects the rights of Patheon or any other indemnitee without Patheon's or such other indemnitee's prior written consent, which shall not be unreasonably withheld or delayed. Patheon's or any other indemnitee's failure to perform any obligations under this Section shall not relieve Client of its obligations hereunder, except to the extent that the Client can demonstrate that it has been materially prejudiced as a result of such failure.

10.5 Reasonable Allocation of Risk.

This Agreement (including, without limitation, this Article 10) is reasonable and creates a reasonable allocation of risk for the relative profits the parties each expect to derive from the Products. Patheon assumes only a limited degree of risk arising from the manufacture, distribution, and use of the Products because Client has developed and holds the marketing approval for the Products, Client requires Patheon to manufacture and label the Products strictly in accordance with the Specifications, and Client, not Patheon, is best positioned to inform and advise potential users about the circumstances and manner of use of the Products.

ARTICLE 11
CONFIDENTIALITY

11.1 Confidential Information.

"**Confidential Information**" means any information disclosed by the Disclosing Party to the Recipient (whether disclosed in oral, written, electronic or visual form) that is non-public, confidential or proprietary including, without limitation, information relating to the Disclosing Party's patent and trademark applications, process designs, process models, drawings, plans, designs, data, databases and extracts therefrom, formulae, methods, know-how and other intellectual property, its clients or client confidential information, finances, marketing, products and processes and all price quotations, manufacturing or professional services proposals, information relating to composition, proprietary technology, and all other information relating to manufacturing capabilities and operations. In addition, all analyses, compilations, studies, reports or other documents prepared by any party's Representatives containing the Confidential Information will be considered Confidential Information. Samples or materials provided hereunder as well as any and all information derived from the approved analysis of the samples or materials will also constitute Confidential Information. Furthermore, any data, reports, information, deliverables, test results, and materials related to the Product generated or made by Patheon under this Agreement (all the foregoing, "**Deliverables**") and Product shall be deemed Confidential Information of Client.

For the purposes of this ARTICLE 11, a party or its Representative receiving Confidential Information under this Agreement is a "**Recipient**," and a party or its Representative disclosing Confidential Information under this Agreement is the **"Disclosing Party**."

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11.2 Use of Confidential Information.

The Recipient will use the Confidential Information solely for the purpose of meeting its obligations under this Agreement. The Recipient will keep the Confidential Information strictly confidential and will not disclose the Confidential Information in any manner whatsoever, in whole or in part, other than to those of its Representatives who (i) have a need to know the Confidential Information for the purpose of this Agreement; (ii) have been advised of the confidential nature of the Confidential Information and (iii) have obligations of confidentiality and non-use to the Recipient no less restrictive than those of this Agreement. Recipient will protect the Confidential Information disclosed to it by using all reasonable precautions to prevent the unauthorized disclosure, dissemination or use of the Confidential Information, which precautions will in no event be less than those exercised by Recipient with respect to its own confidential or proprietary Confidential Information of a similar nature.

11.3 Exclusions.

The obligations of confidentiality will not apply to the extent that the information:

(a) is or becomes publicly known through no breach of this Agreement or fault of the Recipient or its Representatives;

(b) is in the Recipient's possession at the time of disclosure by the Disclosing Party other than as a result of the Recipient's breach of any legal obligation;

(c) is or becomes known to the Recipient on a non-confidential basis through disclosure by sources, other than the Disclosing Party, having the legal right to disclose the Confidential Information, provided that the other source is not known by the Recipient, after due inquiry, to be bound by any obligations (contractual, legal, fiduciary, or otherwise) of confidentiality to the Disclosing Party with respect to the Confidential Information;

(d) is independently developed by the Recipient without use of or reference to the Disclosing Party's Confidential Information as evidenced by Recipient’s written records; or

(e) is expressly authorized for release by the written authorization of the Disclosing Party.

Any combination of information which comprises part of the Confidential Information are not exempt from the obligations of confidentiality merely because individual parts of that Confidential Information were publicly known, in the Recipient’s possession, or received by the Recipient, unless the combination itself was publicly known, in the Recipient’s possession, or received by the Recipient.

11.4 Photographs and Recordings.

Except as required by Law, neither party will take any photographs or videos of the other party’s facilities, equipment or processes, nor use any other audio or visual recording equipment (such as camera phones) while at the other party’s facilities, without that party’s express written consent.

11.5 Permitted Disclosure.

Notwithstanding any other provision of this Agreement, the Recipient may disclose Confidential Information of the Disclosing Party to the extent required, as advised by counsel, in response to a valid order of a court or other governmental body or as required by law, regulation or stock exchange rule. But the Recipient will advise the Disclosing Party in advance of the disclosure to the extent practicable and permissible by the order, law, regulation or stock exchange rule and any other applicable law, will reasonably cooperate with the Disclosing Party, if required, in seeking an appropriate protective order or other remedy, and will otherwise continue to perform its obligations of confidentiality set out herein. If any public disclosure is required by law, the parties will consult concerning the form of announcement prior to the public disclosure being made.

Furthermore, no provision of this Agreement shall be construed so as to preclude disclosure of Patheon Confidential Information by Client as may be reasonably necessary or useful for Client to secure from any Authority necessary marketing or other approvals or licenses for a Product.

Client may disclose this Agreement to one or more third parties (i) in connection with a proposed sale, merger, financing, loan, investment or similar transaction (each a "**Potential Transaction**") so long as those third parties subject to obligations of confidentiality and are limited to using information derived from this Agreement solely for purposes of evaluating whether to enter into one or more of the Potential Transactions and no other purpose.

11.6 Marking.

The Disclosing Party agrees to use reasonable efforts to summarize in writing the content of any oral disclosure or other non-tangible disclosure of Confidential Information within 30 days of the disclosure, but failure to provide this summary will not affect the nature of the Confidential Information disclosed if the Confidential Information was identified as confidential or proprietary when disclosed orally or in any other non-tangible form. Notwithstanding the foregoing, any information which by its nature is confidential and would be judged so under a reasonable standard, or is disclosed, or provided, under circumstances reasonably indicating it is confidential or proprietary, shall be considered Confidential Information regardless of whether a party has marked the Confidential Information as "Confidential" or "Proprietary" or has otherwise identified the information as being confidential.

11.7 Return of Confidential Information.

Upon the written request of the Disclosing Party, the Recipient will promptly return the Confidential Information to the Disclosing Party or, if the Disclosing Party directs, destroy all Confidential Information disclosed in or reduced to tangible form including any copies thereof and any summaries, compilations, analyses or other notes derived from the Confidential Information except for one copy which may be maintained by the Recipient for its records. The retained copy will remain subject to all confidentiality provisions contained in this Agreement.

11.8 Remedies.

The parties acknowledge that monetary damages may not be sufficient to remedy a breach by either party of this Agreement and agree that the non-breaching party will be entitled to seek

specific performance, injunctive and/or other equitable relief (without the need to post bond or other security or to otherwise demonstrate monetary damages) to prevent breaches of this Agreement and to specifically enforce the provisions hereof in addition to any other remedies available at law or in equity. These remedies will not be the exclusive remedies for breach of this Agreement but will be in addition to any and all other remedies available at law or in equity.

ARTICLE 12
DISPUTE RESOLUTION

12.1 Commercial Disputes.

If any dispute arises out of this Agreement or any Product Agreement (other than a dispute under Section 6.1(b) or a Technical Dispute, as defined herein), the parties will first try to resolve it amicably. In that regard, any party may send a notice of dispute to the other, and each party will appoint, within ten Business Days from receipt of the notice of dispute, a single representative having full power and authority to resolve the dispute. The representatives will meet as necessary in order to resolve the dispute. If the representatives fail to resolve the matter within one month from their appointment, or if a party fails to appoint a representative within the ten Business Day period set forth above, the dispute will immediately be referred to the Chief Executive Officer (in the case or Client) or to the Chief Operating Officer (in the case of Patheon), or another officer as he/she may designate, of each party who will meet and discuss as necessary to try to resolve the dispute amicably. Should the parties fail to reach a resolution under this Section 12.1, the dispute will be referred to a court of competent jurisdiction in accordance with Section 13.17.

12.2 Technical Dispute Resolution.

If a dispute arises (other than disputes under Sections 12.1) between the parties that is exclusively related to technical aspects of the manufacturing, packaging, labelling, quality control testing, handling, storage, or other activities under this Agreement (a "**Technical Dispute**"), the parties will make all reasonable efforts to resolve the dispute by amicable negotiations. In that regard, senior representatives of each party will, as soon as possible and in any event no later than ten Business Days after a written request from either party to the other, meet in good faith to resolve any Technical Dispute. If, despite this meeting, the parties are unable to resolve a Technical Dispute within a reasonable time, and in any event within 30 Business Days of the written request, the Technical Dispute will, at the request of either party, be referred for determination to an expert in accordance with Exhibit A. If the parties cannot agree that a dispute is a Technical Dispute, Section 12.1 will prevail. For greater certainty, the parties agree that the release of the Products for sale or distribution under the applicable marketing approval for the Products will not by itself indicate compliance by Patheon with its obligations for the Manufacturing Services and further that nothing in this Agreement (including Exhibit A) will remove or limit the authority of the relevant qualified person (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

12.3 Injunctive Relief.

Nothing in this Article 12 above shall prevent a party from seeking and obtaining temporary or preliminary injunctive or equitable relief to protect the interests of such party pending the outcome of the dispute resolution proceedings set forth above.

ARTICLE 13
MISCELLANEOUS

13.1 Inventions.

(a) For the term of this Agreement, Client hereby grants to Patheon a non-exclusive, paid-up, royalty-free, non-transferable license of Client's Intellectual Property which Patheon must use in order to perform the Manufacturing Services solely for Client.

(b) All Intellectual Property generated or derived by Patheon while performing the Manufacturing Services, to the extent it is specific to the development, manufacture, use, and sale of Client's Product that is the subject of the Manufacturing Services along with all Deliverables (such Intellectual Property and Deliverables collectively, "**Client Arising Intellectual Property**"), will be the exclusive property of Client.

(c) All Patheon Intellectual Property will be the exclusive property of Patheon. Patheon hereby grants to Client [***] to use the Patheon Intellectual Property used by Patheon to perform the Manufacturing Services to enable Client to manufacture the Product(s).

(d) Each party will be solely responsible for the costs of filing, prosecution, and maintenance of patents and patent applications on its own Inventions. Each party will cooperate with the other party in the filing and prosecution of patent applications related to Inventions in which such other party has an ownership interest as a result of activities under this Agreement or otherwise in the registering, perfecting or recording its rights in or to its respective Intellectual Property. Such cooperation will include, but not be limited to, furnishing supporting data and affidavits for the prosecution of patent applications and completing and signing forms needed for the prosecution, assignment and maintenance of patent applications, and causing its personnel (including all subcontractors) to irrevocably waive, to the extent permitted by Law, any and all claims such personnel (including all subcontractors) may now or hereafter have in any jurisdiction to so-called "moral rights" or rights of droit moral.

(e) Either party will give the other party written notice, as promptly as practicable, of all Inventions which can reasonably be deemed to constitute improvements or other modifications of the Products or processes or technology owned or otherwise controlled by the party.

(f) Patheon agrees, and will cause its personnel (including all subcontractors) to agree, that with respect to any Client Arising Intellectual Property that may qualify as "work made for hire" as defined in 17 U.S.C. §101, such Client Arising Intellectual Property are hereby deemed a "work made for hire" for Client. To the extent that any of the Client Arising Intellectual Property do not constitute a "work made for hire", Patheon hereby irrevocably assigns, and shall cause its personnel (including all subcontractors) to irrevocably assign to Client, in each case without additional consideration, all right, title and interest throughout the world in and to the Client Arising Intellectual Property, including all intellectual property rights therein.

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13.2 Intellectual Property.

Subject to Section 13.1, all Client Intellectual Property will be owned by Client and all Patheon Intellectual Property will be owned by Patheon. Neither party has, nor will it acquire, any interest in any of the other party's Intellectual Property unless otherwise expressly agreed to in writing. Neither party will use any Intellectual Property of the other party, except as specifically authorized by the other party or as required for the performance of its obligations under this Agreement.

13.3 Insurance.

Each party will maintain commercial general liability insurance, including blanket contractual liability insurance covering the obligations of that party, including any storage obligations, under this Agreement through the term of this Agreement and for a period of three years thereafter. This insurance will have policy limits of not less than (i) $[***] for each occurrence for personal injury or property damage liability; and (ii) $[***] in the aggregate per annum for product and completed operations liability. If requested each party will give the other a certificate of insurance evidencing the above and showing the name of the issuing company, the policy number, the effective date, the expiration date, and the limits of liability. The insurance certificate will further provide for a minimum of 30 days' written notice to the insured of a cancellation of, or material change in, the insurance. If a party is unable to maintain the insurance policies required under this Agreement through no fault of its own, then the party will forthwith notify the other party in writing and the parties will in good faith negotiate appropriate amendments to the insurance provision of this Agreement in order to provide adequate assurances.

13.4 Independent Contractors.

The parties are independent contractors and this Agreement and any Product Agreement will not be construed to create between Patheon and Client any other relationship such as, by way of example only, that of employer-employee, principal agent, joint-venturer, co-partners, or any similar relationship, the existence of which is expressly denied by the parties. A party shall have no authority to bind or act on behalf of the other Party. This Agreement shall not entitle Patheon to participate in any benefit plan or program of Client. Patheon shall be responsible for, and agrees to comply with, obligations under all applicable tax laws for payment of income and, if applicable, self-employment tax. Patheon is not entitled to worker's compensation coverage by Client, and Patheon hereby waives any and all rights Patheon may have to be covered under Client's worker's compensation policies.

13.5 No Waiver.

Either party's failure to require the other party to comply with any provision of this Agreement or any Product Agreement will not be deemed a waiver of the provision or any other provision of this Agreement or any Product Agreement, with the exception of Sections 6.1 and 8.2 of this Agreement.

13.6 Assignment.

(a) Patheon may not assign this Agreement or any Product Agreement or any of its associated rights or obligations without the written consent of Client, this consent not to be unreasonably withheld. But Patheon may arrange for subcontractors to perform specific testing services arising under any Product Agreement with the consent of Client, not to be unreasonably delayed or withheld. Further it is specifically agreed that Patheon may subcontract any part of the Manufacturing Services under a Product Agreement to any of its Affiliates.

(b) Subject to Section 13.6(a), Client may assign this Agreement or any Product Agreement or any of its associated rights or obligations without approval from Patheon. But Client will give Patheon prior written notice of any assignment, any assignee will covenant in writing with Patheon to be bound by the terms of this Agreement or the Product Agreement, and Client will remain liable hereunder. Any partial assignment of this Agreement or a Product Agreement will be subject to Patheon's cost review of the assigned Products, such review to be performed on an expeditious basis. Client will reimburse Patheon for any costs incurred by Patheon in connection with the partial assignment including any expenses incurred by Patheon for any due diligence audits in connection with the partial assignment.

(c) Despite the foregoing provisions of this Section 13.6, either party may assign this Agreement or any Product Agreement to any of its Affiliates or to a successor to or purchaser of all or substantially all of its business, but the assignee must execute an agreement with the non-assigning party whereby it agrees to be bound hereunder.

13.7 Force Majeure.

Neither party will be liable for the failure to perform its obligations under this Agreement or any Product Agreement if the failure is caused by an event beyond that party's reasonable control, including, but not limited to, strikes, riots, quarantines, communicable disease outbreaks, wars, acts of terrorism, fires, floods, storms, interruption of or delay in transportation, lack of or inability to obtain fuel, power or components, or compliance with any order or regulation of any government entity acting within colour of right provided that that any of these affect the ability to produce or manufacture the Product (a "**Force Majeure Event**"). A party claiming a right to excused performance under this Section 13.7 will immediately notify the other party in writing of the extent of its inability to perform, which notice will specify the event beyond its reasonable control that prevents the performance. The parties may agree to excuse a party from the timelines for payment under this Agreement do to a Force Majeure Event, but such event shall not relieve a party from an obligation to pay money (including any interest for delayed payment) which would otherwise be due and payable under this Agreement or any Product Agreement.

13.8 Additional Product.

Additional Products may be added to, or existing Products deleted from, any Product Agreement by amendments to the Product Agreement including Schedules A, B, C, D, and E as applicable.

13.9 Notices.

Unless otherwise agreed in a Product Agreement, any notice, approval, instruction or other written communication required or permitted hereunder will be sufficient if made or given to the other party by personal delivery, by express delivery (like FedEx, UPS, DHL), by sending the same by certified first class mail, postage prepaid (return receipt requested) to the respective addresses set forth below:

If to Client:

Keryx Biopharmaceuticals, Inc.
One Marina Park Drive, 12th Floor
Boston, MA 02210
Attention: CEO
With a copy (which will not constitute notice) to:
Keryx Biopharmaceuticals, Inc.
One Marina Park Drive, 12th Floor
Boston, MA 02210
Attention: General Counsel

If to Patheon:

[***]
With a copy to:
[***]

or to any other addresses given to the other party in accordance with the terms of this Section 13.9. Notices or written communications made or given by personal delivery will be deemed to have been sufficiently made or given when sent (receipt acknowledged), or if mailed, five days after being deposited in the United States, Canada, or European Union mail, postage prepaid or upon receipt, whichever is sooner. Routine notices relating to invoices, purchase orders and forecasts may be sent by email.

13.10 Severability.

If any provision of this Agreement or any Product Agreement is determined by a court of competent jurisdiction to be invalid, illegal, or unenforceable in any respect, that determination will not impair or affect the validity, legality, or enforceability of the remaining provisions, because each provision is separate, severable, and distinct.

13.11 Entire Agreement.

This Agreement, together with the applicable Product Agreement, and the Quality Agreement, constitutes the full, complete, final and integrated agreement between the parties relating to the subject matter hereof and supersedes all previous written or oral negotiations, commitments,

agreements, transactions, or understandings concerning the subject matter hereof. Any modification, amendment, or supplement to this Agreement or any Product Agreement must be in writing and signed by authorized representatives of both parties. In case of conflict, the prevailing order of documents will be this Agreement, the Product Agreement, and the Quality Agreement.

13.12 Other Terms.

No terms, provisions or conditions of any purchase order or other business form or written authorization used by Client or Patheon will have any effect on the rights, duties, or obligations of the parties under or otherwise modify this Agreement or any Product Agreement, regardless of any failure of Client or Patheon to object to the terms, provisions, or conditions unless the document specifically refers to this Agreement or the applicable Product Agreement and is signed by both parties.

13.13 No Third Party Benefit or Right.

For greater certainty, nothing in this Agreement or any Product Agreement will confer or be construed as conferring on any third party any benefit or the right to enforce any express or implied term of this Agreement or any Product Agreement.

13.14 Execution in Counterparts.

This Agreement and any Product Agreement may be executed in two or more counterparts, by original or facsimile signature, each of which will be deemed an original, but all of which together will constitute one and the same instrument.

13.15 Use of Client Name.

Patheon will not make any use of Client's name, trademarks or logo or any variations thereof, alone or with any other word or words, without the prior written consent of Client.

13.16 Taxes.

(a) The Client will bear all taxes, duties, levies and similar charges (and any related interest and penalties) ("**Tax**" or "**Taxes**"), however designated, imposed as a result of the provision by the Patheon of Services under this Agreement, except:

(i) any Tax based on net income or gross income that is imposed on Patheon by its jurisdiction of formation or incorporation ("**Resident Jurisdiction**");

(i) any Tax based on net income or gross income that is imposed on Patheon by jurisdictions other than its Resident Jurisdiction if this tax is based on a permanent establishment of Patheon; and

(ii) any Tax that is recoverable by Patheon in the ordinary course of business for purchases made by Patheon in the course of providing its Services, such as Value Added Tax (as more fully defined in subparagraph (d) below), Goods & Services Tax ("**GST**") and similar taxes.

(b) If the Client is required to bear a tax, duty, levy or similar charge under this Agreement by any state, federal, provincial or foreign government, including, but not limited to, Value Added Tax, the Client will pay the tax, duty, levy or similar charge and any additional amounts to the appropriate taxing authority as are necessary to ensure that the net amounts received by Patheon hereunder after all such payments or withholdings equal the amounts to which Patheon is otherwise entitled under this Agreement as if the tax, duty, levy or similar charge did not exist.

(c) Patheon will not collect an otherwise applicable tax if the Client's purchase is exempt from Patheon's collection of the tax and a valid tax exemption certificate is furnished by the Client to Patheon.

(d) If subparagraph 13.16 (a)(iii) does not apply, any payment due under this Agreement for the provision of Services to the Client by Patheon is exclusive of value added taxes, turnover taxes, sales taxes or similar taxes, including any related interest and penalties (hereinafter all referred to as "**VAT**"). If any VAT is payable on a Service supplied by Patheon to the Client under this Agreement, this VAT will be added to the invoice amount and will be for the account of (and reimbursable to Patheon by) the Client. If VAT on the supplies of Patheon is payable by the Client under a reverse charge procedure (i.e., shifting of liability, accounting or payment requirement to recipient of supplies), the Client will ensure that Patheon will not effectively be held liable for this VAT by the relevant taxing authorities or other parties. Where applicable, Patheon will use its reasonable commercial efforts to ensure that its invoices to the Client are issued in such a way that these invoices meet the requirements for deduction of input VAT by the Client, if the Client is permitted by law to do so.

(e) Unless consented to by Patheon (such consent not to be unreasonably withheld, conditioned or delayed), any Tax that Client pays, or is required to pay, but which Client believes should properly be paid by Patheon pursuant hereto may not be offset against sums due by Client to Patheon whether due pursuant to this Agreement or otherwise. Further, for any Tax remitted by Client but as to which Patheon is liable hereunder, if so requested by Client, Patheon shall promptly reimburse Client for such amounts paid on Patheon's behalf.

13.17 Governing Law.

This Agreement and any Product Agreement, unless otherwise agreed by the parties in the Product Agreement, will be construed and enforced in accordance with the laws of the State of New York and the laws of the United States of America applicable therein, without application of conflicts of laws provisions that would otherwise apply the substantive law of another jurisdiction. Subject to the alternative dispute resolutions provision set forth in Article 12 above, any legal suit, action or proceeding arising out of or related to this Agreement or the services provided hereunder shall be instituted exclusively in the federal courts of the United States or the courts of the State of New York, in each case located in New York County, New York, and each party irrevocably submits to the exclusive jurisdiction of

such courts in any such suit, action or proceeding. The UN Convention on Contracts for the International Sale of Goods will not apply to this Agreement.

[Signature page to follow]

IN WITNESS WHEREOF, the duly authorized representatives of the parties have executed this Agreement as of the Effective Date.

PATHEON MANUFACTURING SERVICES LLC
By: /s/ [***]
Name: [***]
Title: Director, Business Management

KERYX BIOPHARMACEUTICALS, INC.
By: /s/ Greg Madison
Name: Greg Madison
Title: President & CEO

Exhibit 10.64

AMENDMENT NO. 4 TO
MASTER MANUFACTURING SERVICES AND SUPPLY AGREEMENT

This Amendment No. 4 to Master Manufacturing Services and Supply Agreement ("Amendment No. 4") is made effective and entered into on December 17, 2021 (the "Amendment Effective Date") by and between **Siegfried Evionnaz SA**, with principal offices located at Route du Simplon 1, 36, 1902 Evionnaz, Switzerland (together with its Affiliates and subsidiaries "Vendor"); and **Keryx Biopharmaceuticals, Inc.**, with its offices at 245 First Street, Cambridge, Massachusetts, USA 02142 ("Keryx").

WHEREAS, Vendor and Keryx entered into a Master Manufacturing Services and Supply Agreement dated December 20, 2017 ("Agreement") under which Vendor manufactures Product for purchase by Keryx; and

WHEREAS, on December 12, 2018, Keryx merged with Akebia Therapeutics, Inc. ("Akebia") and, pursuant to such merger, Akebia assumed all of Keryx's rights and obligations under the Agreement. Keryx continues to operate as a wholly owned subsidiary of Akebia, and Akebia is an Affiliate of Keryx; and

WHEREAS, Vendor and Keryx wish to amend the Agreement as herein provided;

NOW THEREFORE, Vendor and Keryx hereto mutually agree as follows:

1. The text of Section 16.1.1 of the Agreement is be deleted and is hereby replaced by the following:

   16.1.1 The term of this Agreement (the "Term") shall commence as of the Agreement Date and, subject to earlier termination in accordance with the provisions of this Section 16, shall end on December 31, 2022 unless otherwise agreed by the Parties. Notwithstanding the foregoing, Keryx may elect to extend the Term through December 31, 2023 with written notice sent at least eleven (11) months prior to the expiry of the Term, in accordance with Section 22 herein. In the event of such an election by Keryx, Keryx's Minimum Annual Purchase Obligation for 2023 set forth in Attachment B shall apply. For the avoidance of doubt, expiration of the Term in accordance with this Section 16.1.1 shall not relieve Keryx of its responsibilities to pay any undisputed invoices issued by Vendor for Product or other Services performed in accordance with Section 3 of the Agreement.

2. For the purpose of this Amendment No. 4, the defined terms used herein shall have the same meaning as those used in the Agreement, unless otherwise specified in this Amendment No. 4.

3. Except as provided for in this Amendment No. 4, all other terms and conditions of the Agreement shall remain in full force and effect.

4. The governing law and jurisdiction applicable to the Agreement shall apply to this Amendment No. 4.

[Signature page follows]

IN WITNESS WHEREOF, Vendor and Keryx hereto have caused this Amendment No. 2 to be executed by their duly authorized representatives as of the date first above written.

Signed on behalf of Siegfried Evionnaz SA

By: /s/ Shawn Springfield
Name: Shawn Springfield

Date: 17-Dec-2021

Signed on behalf of Keryx Biopharmaceuticals, Inc.

By: /s/ Michel Dahan
Name: Michel Dahan, SVP, Chief Operating Officer

Date: 17-Dec-2021

Signed on behalf of Siegfried Evionnaz SA

By: /s/ Luca Parlanti
Name: Luca Parlanti

Date: 17-Dec-2021

Exhibit 10.69

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

FIRST AMENDMENT AND WAIVER

This FIRST AMENDMENT AND WAIVER (this "Amendment and Waiver"), dated and effective as of February 18, 2022 (the "Effective Date"), by and among AKEBIA THERAPEUTICS, INC., a Delaware corporation (as "Borrower"), BIOPHARMA CREDIT PLC, a public limited company incorporated under the laws of England and Wales (as the "Collateral Agent"), BPCR LIMITED PARTNERSHIP, a limited partnership established under the laws of England and Wales (as a "Lender"), and BIOPHARMA CREDIT INVESTMENTS V (MASTER) LP, a Cayman Islands exempted limited partnership (as a "Lender").

Recitals

A. Collateral Agent, Lenders, Borrower and the other Credit Parties thereunder have entered into that certain Loan Agreement, dated as of November 11, 2019 (the "Loan Agreement").

B. Borrower desires to enter into that certain Second Amended and Restated License Agreement (the "License Agreement") with Vifor (International) Ltd. ("Vifor"), pursuant to which Vifor will provide to Borrower, and Borrower will incur, Indebtedness in the form of a working capital loan, as described in greater detail in Section 11.5 of the License Agreement (the "Working Capital Loan").

C. Pursuant to Section 6.4 of the Loan Agreement, the Working Capital Loan does not constitute Permitted Indebtedness.

D. In connection with Borrower's obligation to deliver to the Collateral Agent annual consolidated financial statements which are audited by an independent certified public accounting firm of recognized national standing, Section 5.2(a)(i)(x) of the Loan Agreement requires Borrower to deliver to the Collateral Agent a report and opinion of such certified public accounting firm which are prepared in accordance with Applicable Accounting Standards and , with respect to any period ending after September 30, 2020, are not subject to any qualification as to "going concern" or scope of audit (the "Accountant Opinion Covenant").

E. Borrower has become aware that the opinion of its independent certified public accounting firm accompanying Borrower's consolidated financial statements for the fiscal year ending December 31, 2021 may be subject to certain qualifications, including a "going concern" qualification.

F. In accordance with Section 11.5 of the Loan Agreement, Borrower and Lenders desire to amend the Loan Agreement to, among other things, permit the Working Capital Loan, and Lenders agree to provide Borrower with a waiver of the no "going concern" qualification requirement in the Accountant Opinion Covenant, in each case on the terms and conditions set forth herein.

Agreement

Now, Therefore, in consideration of the foregoing recitals and other good and valuable consideration, the receipt and adequacy of which is hereby acknowledged, and intending to be legally bound, the parties hereto agree as follows:

1. Definitions. All capitalized terms used in this Amendment and Waiver (including in the recitals hereof) and not otherwise defined herein shall have the meanings assigned to them in the Loan Agreement. The rules of interpretation set forth in the first paragraph of Section 13.1 of the Loan Agreement shall be applicable to this Amendment and Waiver and are incorporated herein by this reference.

2. Amendment to Loan Agreement.

a. The Loan Agreement shall be amended by adding the following sub-clause (iii) to Section 2.2(c) of the Loan Agreement:

"(iii) Prior to any prepayment, repayment, repurchase or redemption, in whole or in part, of the Indebtedness described in clause (c) of the definition of Permitted Indebtedness, whether or not [**] (a "**Working Capital Loan Repayment**"), Borrower shall promptly, and in any event no later than [**] prior to the date on which such Indebtedness (or portion thereof) is due to be prepaid, repaid, repurchased or redeemed (the "**Working Capital Loan Repayment Date**"), notify the Collateral Agent in writing of such Working Capital Loan Repayment, which notice shall include reasonable detail as to the nature, timing and other circumstances of such prepayment, repayment, repurchase or redemption (such notice, a "**Working Capital Loan Repayment Notice**"); provided, however, that [**]. In the event of a Working Capital Loan Repayment, Borrower shall prepay in full all of the Term Loans advanced by Lenders under this Agreement no later than [**] prior to the Working Capital Loan Repayment Date in an amount equal to the sum of (A) all unpaid principal and any and all accrued and unpaid interest with respect to the Term Loans (or such remaining outstanding portion thereof), and (B) any applicable amounts payable with respect to the prepayment under this Section 2.2(c)(iii) pursuant to Section 2.2(e) or Section 2.2(f) and all other amounts payable or accrued and not yet paid under this Agreement and the other Loan Documents. The Collateral Agent will promptly notify each Lender of its receipt of the Working Capital Loan Repayment Notice, and the amount of such Lender's Applicable Percentage of such prepayment of the Term Loans.

b. The Loan Agreement shall be amended by deleting the phrase "pursuant to Section 2.2(c)(i) or Section 2.2(c)(ii)," appearing in each of Section 2.2(e)(i), Section 2.2(e)(ii), Section 2.2(f)(i) and Section 2.2(f)(ii) of the Loan Agreement and replacing it in each such Section with the phrase "pursuant to Section 2.2(c)(i), Section 2.2(c)(ii) or Section 2.2(c)(iii),".

c. The Loan Agreement shall be amended by deleting the phrase "Section 2.2(c)(ii)" in each place it appears in Section 7.1 of the Loan Agreement and replacing it with the phrase "Section 2.2(c)(ii) or Section 2.2(c)(iii)".

d. The Loan Agreement shall be amended by deleting in its entirely Section 5.2(a)(ii) of the Loan Agreement and replacing it as follows:

"(ii) Quarterly Financial Statements. As soon as available, but in any event within [**] after the end of each of the first three (3) fiscal quarters of each fiscal year of Borrower (or such earlier date on which Borrower is required to file a Form 10-Q under the Exchange Act, as applicable), beginning with the fiscal quarter ending March 31, 2020, a consolidated balance sheet of Borrower and its Subsidiaries as of the end of such fiscal quarter, and the related consolidated statements of income and cash flows and for such fiscal quarter and (in respect of the second and third fiscal quarters of such fiscal year) for the then-elapsed portion of Borrower's fiscal year,

setting forth in each case in comparative form the figures for the comparable period or periods in the previous fiscal year, all prepared in accordance with Applicable Accounting Standards, and for the fiscal quarters ending June 30, 2022 and September 30, 2022, not subject to any qualification as to "going concern", subject to normal year-end audit adjustments and the absence of disclosures normally made in footnotes; provided, however, that Borrower shall be deemed to have made such delivery of such consolidated financial statements if such consolidated financial statements shall have been made available within the time period specified above on the SEC's EDGAR system (or any successor system adopted by the SEC). Such consolidated financial statements shall be certified by a Responsible Officer of Borrower as, to his or her knowledge, fairly presenting, in all material respects, the consolidated financial condition, results of operations and cash flows of Borrower and its Subsidiaries as of the dates and for the periods specified in accordance with Applicable Accounting Standards consistently applied, and on a basis consistent with the audited consolidated financial statements referred to under Section 5.2(a)(i), subject to normal year-end audit adjustments and the absence of footnotes; provided, however, that such certification by a Responsible Officer of Borrower shall be deemed to have made if a similar certification is required under the Sarbanes-Oxley Act of 2002 and such certificate shall have been made available within the time period specified above on the SEC's EDGAR system (or any successor system adopted by the SEC);".

e. The Loan Agreement shall be amended by deleting in its entirety clause (c) of the definition of Permitted Indebtedness in Section 13.1 of the Loan Agreement and replacing it as follows:

"(c) Indebtedness of Borrower [**] consisting of working capital payments funded pursuant to Section 11.5 of the Vifor License Agreement, provided, that such Indebtedness [**]."

f. The Loan Agreement shall be amended by adding the following definitions to Section 13.1 of the Loan Agreement:

""**Vifor License Agreement**" means that certain Second Amended and Restated License Agreement, dated as of February 18, 2022 between Borrower and Vifor (International) Ltd., as may be amended from time to time."

""**Working Capital Loan Repayment**" is defined in Section 2.2(c)(iii)."

""**Working Capital Loan Repayment Date**" is defined in Section 2.2(c)(iii)."

""**Working Capital Loan Repayment Notice**" is defined in Section 2.2(c)(iii)."

3. Representations and Warranties; Reaffirmation.

a. Borrower hereby represents and warrants to each Lender and the Collateral Agent as follows:

i. Borrower has all requisite power and authority to enter into this Amendment and Waiver and to carry out the transactions contemplated hereby.

ii.This Amendment and Waiver has been duly executed and delivered by Borrower and is the legally valid and binding obligation of Borrower,

enforceable against Borrower in accordance with its respective terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws relating to or limiting creditors' rights generally or by general principles of equity.

iii. The execution, delivery and performance by Borrower of this Amendment and Waiver have been duly authorized and do not: (A) contravene the terms of any of Borrower's Operating Documents; (B) violate any Requirements of Law, except to the extent that such violation could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change; (C) conflict or result in any breach or contravention of, or require any payment to be made under any provision of any security issued by Borrower or of any agreement, instrument or other undertaking to which Borrower is a party or affecting Borrower or the assets or properties of Borrower or any of its Subsidiaries or any order, writ, judgment, injunction, decree, determination or award of any Governmental Authority by which Borrower or any of its assets or properties are subject, except to the extent that such conflict, breach, contravention or payment could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change; (D) require any Governmental Approval or other action by, or notice to, or filing with, any Governmental Authority (except such Governmental Approvals or other actions, notices and filings which have been duly obtained, taken, given or made on or before the Effective Date and are in full force and effect); (E) require any approval, consent, exemption or authorization, or other action by, or notice to, or filing with, any Person other than a Governmental Authority, including Borrower's stockholders, members or partners, (except such approvals, consents, exemptions, authorizations, actions, notices and filings which have been or will be duly obtained, taken, given or made on or before the Effective Date and are in full force and effect), except for those approvals, consents, exemptions, authorizations or other actions, notices or filings, the failure of which to obtain or make could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change; or (F) constitute a material breach of or a material default under (which such default has not been cured or waived) or an event of default (or the equivalent thereof, however described) under, or could reasonably be expected to give rise to the cancellation, termination or invalidation of or the acceleration of Borrower's or any Subsidiary's obligations under, any Material Contract.

b. Borrower hereby ratifies, confirms, reaffirms, and acknowledges its obligations under the Loan Documents to which it is a party and agrees that the Loan Documents remain in full force and effect, undiminished by this Amendment and Waiver, except as expressly provided herein. By executing this Amendment and Waiver, Borrower acknowledges that it has read, consulted with its attorneys regarding, and understands, this Amendment and Waiver.

4. **Waivers.** As of the Effective Date, the requirement that the annual audit opinion required to be delivered by Borrower to the Collateral Agent not be subject to a "going concern"

qualification in Section 5.2(a)(i)(x) of the Loan Agreement is hereby waived solely for the fiscal year ending December 31, 2021.

5. Limitation of Waivers. The waivers set forth above shall be limited precisely as written and relate solely to the provisions of Section 5.2(a)(i)(x) of the Loan Agreement and Section 5.2(a)(ii) of the Loan Agreement (as amended by this Amendment and Waiver), respectively, in the manner and to the extent described above and nothing in this Amendment and Waiver shall be deemed to:

a. Constitute a waiver of compliance by Borrower or any other Credit Party with respect to any other term, provision or condition of the Loan Agreement or any other Loan Document, or any other instrument or agreement referred to therein; or

b. Prejudice any right or remedy that the Collateral Agent or any Person that is a lender at any time under the Loan Agreement may now have or may have in the future under or in connection with the Loan Agreement or any other Loan Document, or any other instrument or agreement referred to therein.

6. References to and Effect on Loan Agreement. Except as specifically set forth herein, this Amendment and Waiver shall not modify or in any way affect any of the provisions of the Loan Agreement, which shall remain in full force and effect and is hereby ratified and confirmed in all respects. On and after the Effective Date, all references in the Loan Agreement to "this Agreement," "hereto," "hereof," "hereunder," or words of like import shall mean the Loan Agreement as amended by this Amendment and Waiver.

7. Successors and Assigns. This Amendment and Waiver shall inure to the benefit of and be binding upon the Borrower, Credit Parties, Lenders, Collateral Agent and the banks and other financial institutions from time to time parties to the Loan Agreement, and each of their respective successors and assigns.

8. Governing Law; Venue; Jury Trial Waiver. THIS AMENDMENT AND WAIVER SHALL BE GOVERNED BY, AND CONSTRUED AND INTERPRETED IN ACCORDANCE WITH, THE LAWS OF THE STATE OF NEW YORK, WITHOUT REGARD TO ANY PRINCIPLES OF CONFLICTS OF LAW THAT COULD REQUIRE THE APPLICATION OF THE LAW OF ANY OTHER JURISDICTION. Each of Borrower and each other Credit Party submits to the exclusive jurisdiction of the courts of the State of New York sitting in New York County, and of the United States District Court of the Southern District of New York, and any appellate court from any thereof, and agrees that all claims in respect of any such action, litigation or proceeding may be heard and determined in such New York State court or, to the fullest extent permitted by Requirements of Law, in such Federal court; provided, however, that nothing in this Amendment and Waiver shall be deemed to operate to preclude the Collateral Agent or any Lender from bringing suit or taking other legal action in any other jurisdiction to realize on the Collateral or any other security for the Obligations, or to enforce a judgment or other court order in favor of the Collateral Agent or any Lender. Each of Borrower and each other Credit Party expressly submits and consents in advance to such jurisdiction in any action or suit commenced in any such court, and each of Borrower and each other Credit Party hereby waives any objection that it may have based upon lack of personal jurisdiction, improper venue, or forum non conveniens and hereby consents to the granting of such legal or equitable relief as is deemed appropriate by such court. Each of Borrower and each other Credit Party hereby waives personal service of the summons, complaints, and other process issued in such action or suit and agrees that service of such summons, complaints, and other process may be made by registered or certified mail addressed to such party at the address set forth in (or

otherwise provided in accordance with the terms of) Section 9 of the Loan Agreement as amended by this Amendment and Waiver and that service so made shall be deemed completed upon the earlier to occur of such party's actual receipt thereof or three (3) days after deposit in the U.S. mails, proper postage prepaid.

TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, EACH OF BORROWER, EACH OTHER CREDIT PARTY, LENDERS AND THE COLLATERAL AGENT WAIVES ITS RIGHT TO A JURY TRIAL OF ANY CLAIM OR CAUSE OF ACTION ARISING OUT OF OR BASED UPON THIS AMENDMENT AND WAIVER OR ANY TRANSACTION CONTEMPLATED HEREBY, INCLUDING CONTRACT, TORT, BREACH OF DUTY AND ALL OTHER CLAIMS. THE WAIVER SET FORTH IN THIS SECTION 8 IS A MATERIAL INDUCEMENT FOR ALL PARTIES HERETO TO ENTER INTO THIS AMENDMENT AND WAIVER. EACH PARTY HERETO HAS REVIEWED THIS AMENDMENT AND WAIVER WITH ITS COUNSEL.

9. Counterparts. This Amendment and Waiver may be executed in any number of counterparts, all of which shall constitute one and the same agreement, and any party hereto may execute this Amendment and Waiver by signing and delivering one or more counterparts. Delivery of an executed counterpart of this Amendment and Waiver electronically or by facsimile shall be effective as delivery of an original executed counterpart of this Amendment and Waiver.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the undersigned hereto have caused this Amendment and Waiver to be executed as of the date first written above by each of their officers thereunto duly authorized.

BORROWER (on its own behalf and on behalf of each other Credit Party):

AKEBIA THERAPEUTICS, INC.,
a Delaware corporation

By: /s/ David Spellman
Name: David Spellman
Title: Senior Vice President, Chief Financial Officer and Treasurer

BIOPHARMA CREDIT PLC,
as Collateral Agent

By: Pharmakon Advisors, LP,
its Investment Manager

By: Pharmakon Management I, LLC,
its General Partner

By /s/ Pedro Gonzalez de Cosio
Name: Pedro Gonzalez de Cosio
Title: Managing Member

BPCR LIMITED PARTNERSHIP,
as a Lender

By: Pharmakon Advisors, LP,
its Investment Manager

By: Pharmakon Management I, LLC,
its General Partner

By /s/ Pedro Gonzalez de Cosio
Name: Pedro Gonzalez de Cosio
Title: Managing Member

BIOPHARMA CREDIT INVESTMENTS V (MASTER) LP,
as Lender

By: BioPharma Credit Investments V GP LLC,
its general partner

By: Pharmakon Advisors, LP,
its Investment Manager

By /s/ Pedro Gonzalez de Cosio
Name: Pedro Gonzalez de Cosio
Title: CEO and Managing Member

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-196748) pertaining to the Amended and Restated 2008 Equity Incentive Plan, the 2014 Incentive Plan, and the 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(2) Registration Statement (Form S-8 No. 333-209469) pertaining to the 2014 Incentive Plan and the 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(3) Registration Statement (Form S-8 No. 333-216475) pertaining to the 2014 Incentive Plan and the 2016 Inducement Award Program of Akebia Therapeutics, Inc.,

(4) Registration Statement (Form S-8 No. 333-222728) pertaining to the 2014 Incentive Plan and the 2016 Inducement Award Program of Akebia Therapeutics, Inc.,

(5) Registration Statement (Form S-4 No. 333-227622) of Akebia Therapeutics, Inc.,

(6) Registration Statement (Form S-8 No. 333-228772) pertaining to the 2014 Incentive Plan of Akebia Therapeutics, Inc. and the 1999 Share Option Plan, 2004 Long-Term Incentive Plan, 2007 Incentive Plan, Amended and Restated 2013 Incentive Plan, and 2018 Equity Incentive Plan of Keryx Biopharmaceuticals, Inc.,

(7) Registration Statement (Form S-8 No. 333-229366) pertaining to the 2014 Incentive Plan, the 2014 Employee Stock Purchase Plan, and the Inducement Grants (January 2018 – December 2018) of Akebia Therapeutics, Inc.,

(8) Registration Statement (Form S-8 No. 333-233140) pertaining to the amended and restated 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(9) Registration Statement (Form S-8 No. 333-236060) pertaining to the 2014 Incentive Plan and the Inducement Grant Awards (January 2019 – December 2019) of Akebia Therapeutics, Inc., and

(10) Registration Statement (Form S-8 No. 333-252336) pertaining to the 2014 Incentive Plan and the Inducement Grant Awards (January 2020 – December 2020) of Akebia Therapeutics, Inc.,

(11) Registration Statement (Form S-3 No. 333-253539) of Akebia Therapeutics, Inc., and

(12) Registration Statement (Form S-8 No. 333-262392) pertaining to the 2014 Incentive Plan and the Inducement Grant Awards (January 2021 – December 2021) of Akebia Therapeutics, Inc.;

of our reports dated March 1, 2022, with respect to the consolidated financial statements of Akebia Therapeutics, Inc. and the effectiveness of internal control over financial reporting of Akebia Therapeutics, Inc. included in this Annual Report (Form 10-K) of Akebia Therapeutics, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 1, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, John P. Butler, certify that:

1. I have reviewed this Annual Report on Form 10-K of Akebia Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the Audit Committee of the registrant's Board of Directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2022

By: /s/ John P. Butler
John P. Butler
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David A. Spellman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Akebia Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the Audit Committee of the registrant's Board of Directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2022

By: /s/ David A. Spellman
David A. Spellman
Senior Vice President, Chief Financial Officer
and Treasurer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. Section 1350)

In connection with the accompanying Annual Report of Akebia Therapeutics, Inc. (the Company) on Form 10-K for the fiscal year ended December 31, 2021 (the Report), I, John P. Butler, as Chief Executive Officer and President of the Company, and I, David A. Spellman, as Senior Vice President, Chief Financial Officer and Treasurer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date:	March 1, 2022	By:	/s/ John P. Butler John P. Butler President, Chief Executive Officer and Director (Principal Executive Officer)
Date:	March 1, 2022	By:	/s/ David A. Spellman David A. Spellman Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer)